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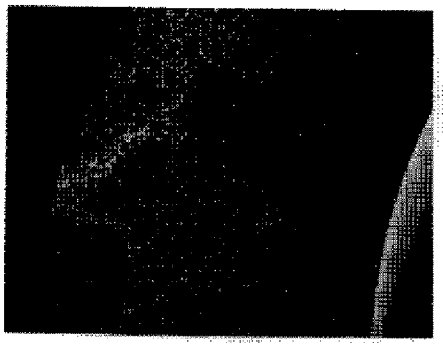
(54)【発明の名称】　ポリスルホン系中空繊維膜とその製造方法

(57)【要約】

【目的】　生体適応性に優れ、かつ乾燥した後に透水性の低下のない、特に血液処理に適したポリスルホン系中空繊維膜とその製造方法を提供する。

【構成】　ポリスルホン系ポリマーからなる、内表面に緻密層をもつ非対称構造の中空繊維膜であって、該中空繊維膜はポリグリコール類を１重量%以上、ビニルピロリドン系ポリマーを１～８重量%含有し、かつ中空繊維膜の内表面緻密層に存在するポリスルホン系ポリマーとビニルピロリドン系ポリマーの重量比率が90：10～60：40で、しかも中空繊維膜の内表面緻密層に存在するビニルピロリドン系ポリマーの重量比率が外表面層に存在するビニルピロリドン系ポリマーの重量比率の少なくとも1.1倍であるポリスルホン系中空繊維膜。

図面代用写真



(写真)

【特許請求の範囲】

【請求項１】　ポリスルホン系ポリマーからなる、内表面に緻密層をもつ非対称構造の中空繊維膜であって、該中空繊維膜はポリスルホン系ポリマーを主成分とし、少なくとも１重量%のポリグリコール類と１～８重量%のビニルピロリドン系ポリマーを含有し、かつ中空繊維膜の内表面の緻密層に存在するポリスルホン系ポリマーとビニルピロリドン系ポリマーの重量比率が90：10～60：40で、しかも中空繊維膜の内表面の上記緻密層に存在するビニルピロリドン系ポリマーの重量比率が外表面層に存在するビニルピロリドン系ポリマーの重量比率の少なくとも 1.1倍であることを特徴とするポリスルホン系中空繊維膜。

【請求項２】　上記ポリグリコール類がポリエチレングリコールである請求項１に記載のポリスルホン系中空繊維膜。

【請求項３】　上記ビニルピロリドン系ポリマーがポリビニルピロリドン、ビニルピロリドン・酢酸ビニル共重合体、ビニルピロリドン・ビニルアルコール共重合体、ビニルピロリドン・スチレン共重合体、ビニルピロリドン・ジメチルアミノエチルメタクリレート共重合体およびこれらの変性ポリマーよりなる群から選ばれる請求項１または２に記載のポリスルホン系中空繊維膜。

【請求項４】　中空繊維膜の内表面の緻密層に存在するビニルピロリドン系ポリマーの重量比率が外表面層に存在するビニルピロリドン系ポリマーの重量比率の少なくとも 1.5倍である請求項１ないし３の何れかに記載のポリスルホン系中空繊維膜。

【請求項５】　中空繊維膜の内表面の緻密層に存在するビニルピロリドン系ポリマーの重量比率が外表面層に存在するビニルピロリドン系ポリマーの重量比率の少なくとも 2.0倍である請求項１ないし４の何れかに記載のポリスルホン系中空繊維膜。

【請求項６】　ポリスルホン系ポリマーと重量平均分子量 200～ 6,000のポリグリコール類および重量平均分子量が少なくとも10,000のビニルピロリドン系ポリマーとを混合溶解した製膜原液を環状オリフィスより吐出させる工程と、 0.1～４重量%のビニルピロリドン系ポリマーを含有する溶液を上記吐出原液の環状の流れの内部に供給してポリスルホン系中空繊維膜を形成する工程と、該製膜されたポリスルホン系中空繊維膜を、該ポリスルホン系ポリマーに対して貧溶媒作用を有する溶液で処理して、中空繊維膜の内表面の緻密層に存在するビニルピロリドン系ポリマーの重量比率が外表面層に存在するビニルピロリドン系ポリマーの重量比率の少なくとも 1.1倍となるように調整する工程とを含んでなることを特徴とするポリスルホン系中空繊維膜の製造方法。

【請求項７】　上記ポリグリコール類がポリエチレングリコールである請求項６に記載のポリスルホン系中空繊維膜の製造方法。

【請求項８】　上記ビニルピロリドン系ポリマーがポリビニルピロリドン、ビニルピロリドン・酢酸ビニル共重合体、ビニルピロリドン・ビニルアルコール共重合体、ビニルピロリドン・スチレン共重合体、ビニルピロリドン・ジメチルアミノエチルメタクリレート共重合体およびこれらの変性ポリマーよりなる群から選ばれる請求項６または７に記載のポリスルホン系中空繊維膜の製造方法。

【請求項９】　上記ポリスルホン系ポリマーに対して貧溶媒作用を有する溶液が水、アルコール類、エチレングリコール、プロピレングリコール、グリセリン、重量平均分子量 600以下のポリエチレングリコールよりなる群から選ばれる少なくとも１種の液体である請求項６ないし９の何れかに記載のポリスルホン系中空繊維膜の製造方法。

【請求項１０】　中空繊維膜の内表面の緻密層に存在するビニルピロリドン系ポリマーの重量比率が外表面層に存在するビニルピロリドン系ポリマーの重量比率の少なくとも 1.5倍となるように、ポリスルホン系中空繊維膜を該ポリスルホン系ポリマーに対して貧溶媒作用を有する溶液で処理して調整する請求項６ないし９に記載のポリスルホン系中空繊維膜の製造方法。

【請求項１１】　中空繊維膜の内表面の緻密層に存在するビニルピロリドン系ポリマーの重量比率が外表面層に存在するビニルピロリドン系ポリマーの重量比率の少なくとも２倍となるように、ポリスルホン系中空繊維膜を該ポリスルホン系ポリマーに対して貧溶媒作用を有する溶液で処理して調整する請求項６ないし10に記載のポリスルホン系中空繊維膜の製造方法。

【発明の詳細な説明】

【０００１】

【産業上の利用分野】本発明はポリスルホン系中空繊維膜およびその製造方法、特に中空繊維膜の内表面の緻密層にビニルピロリドン系ポリマーを多量に存在させた、血液処理に適したポリスルホン系中空繊維膜およびその製造方法に関するものである。

【０００２】

【従来の技術】近年、選択透過性分離膜を用いた分離技術である限外濾過法、逆浸透法、気体分離法等が各種の分野において実用化されており、その多様な用途に各々適する素材から作られた分離膜が上市されている。選択透過性分離膜の素材としては、セルロース系、セルロースアセテート系、ポリアミド系、ポリアクリロニトリル系、ポリビニルアルコール系、ポリメチルメタクリレート系、ポリスルホン系、ポリオレフィン系などのポリマーが使用されている。中でもポリスルホン系ポリマーは、耐熱性、耐酸性、耐アルカリ性、耐酸化性などの物理化学的性質が優れていることから、最近医療用、工業用分離膜の素材として注目されている。

【０００３】しかしながら、ポリスルホン系ポリマーは

疎水性の素材であるために、これを素材とした選択透過性分離膜は親水性ポリマーを素材とした選択透過性分離膜に比べて、水濡れ性が悪く、また乾燥すると性能が低下する。そこでポリスルホン系ポリマーからなる選択透過性分離膜に親水性を付与して水濡れ性を向上させるための検討がなされ、その一つの方法として、ポリスルホン系ポリマー等の疎水性ポリマーからなる分離膜に、ポリビニルピロリドン等の親水性ポリマーを含有させた選択透過性分離膜とその製法が提案されている。

【０００４】例えば特公平2-18695 号にはポリスルホン、分子量10万以上のポリビニルピロリドンおよびそれらの共通溶媒からなる原液を紡糸して製造された、分離膜内に分子量10万以上のポリビニルピロリドンを５～70重量%含有させ、かつ11%以上の吸水能力を有するポリスルホン系分離膜とその製法が開示されている。特開昭61-93801号には疎水性ポリマー、親水性ポリマーおよびそれらの共通溶媒からなる低粘度の原液を紡糸することにより製造された、親水性ポリマーを１～10重量%含有させ、かつ３～10%の吸水能力を有する血液処理用の中空繊維膜とその製法が開示されている。

【０００５】特開昭61-238306 号、同63-97666号にはポリスルホン系ポリマー、親水性ポリマー、該ポリスルホン系ポリマーに対して非溶媒もしくは膨潤剤なる添加剤を加えた系を製膜原液として用いたポリスルホン系分離膜の製造方法が開示されている。また特開昭63-97205号、同63-97634号には、上記方法で製造されたポリスルホン系分離膜に放射線処理および／または熱処理を施すことによって親水性ポリマーを不溶化する方法が開示されている。さらに特開昭63-99325号には上記製膜原液を用いて紡糸する際に、水溶性ポリマーを少なくとも５重量%含有する注入液を使用して内表面を滑らかとしたポリスルホン系中空糸膜が開示されている。

【０００６】特開昭61-238834 号、同63-99325号には、上記製造法により得られた平均孔径が500 オングストローム以上の細孔を持ち、かつ親水性ポリマーを３～30重量%含有する透水量が1000 ml/m^2・hr・mmHg以上であるポリスルホン系多孔膜が開示されている。特開昭61-402号、同62-38205号には、非対称構造を有する疎水性ポリマーからなる分離膜の緻密層側だけが、該疎水性ポリマーと親水性ポリマーとの混合物からなる分離膜が開示されている。

【０００７】

【発明が解決しようとする課題】上記ポリスルホン系分離膜は膜内に親水性ポリマーを存在させることにより疎水性のポリスルホン系分離膜に水濡れ性を付与し、かつ透水性能を向上させ、しかも、蛋白吸着等による膜の汚染が防止される等の優れた性能を有しているが、生体適合性についての十分な検討がなされておらず、抗血栓性の点で必ずしも満足されるものではない。

【０００８】例えば特開昭61-93801号には血液処理に適したポリスルホン系中空繊維膜が開示されている。かかる中空繊維膜について明細書中には補体活性を低く抑えることができる膜である旨の記載があるが、補体活性が低く抑えられるという特性は中空繊維膜が疎水性であることによってのみ発現される性質である。すなわち特開昭61-93801号に開示された中空繊維膜は血液が接触する内表面が十分に親水化されておらず、依然として疎水性が残っていることを示唆している。血液が接触する表面に疎水性が残っていると血小板が付着しやすい状態にある。いったん中空繊維膜の内表面に血小板が付着すると、血小板の凝集、崩壊により血液凝固系を活性化する物質が放出されて血液凝固が生じる。

【０００９】また特公平2-18695 号に開示されたポリスルホン系分離膜は11%以上の吸水能を有しているので、製膜後の保存中に空気中の水分を吸収する。そのため分離膜保存のために特別な設備が必要となる。また吸水能が高いことは、分離膜内のポリビニルピロリドンの存在量が多いため、分離膜の機械的性能が低下し、透水性能も低下する。

【００１０】さらに特開昭61-238306 号、特開昭63-99325号等で開示されたポリスルホン系分離膜の製法あるいは特開昭61-238834 号等で開示されたポリスルホン系分離膜は、製膜原液に親水性ポリマーを添加しているため、特開昭61-93801号に開示されたポリスルホン系中空繊維膜と同様に分離膜の内表面を十分に親水化することができない。またかかる製法は 500オングストローム以上の大きな孔を有する分離膜の製法に適しているが、血液透析用の分離膜の製法には適当でない。特開昭63-99325号に開示されたポリスルホン系分離膜の製法は内部凝固液中に水溶性ポリマーを含有させているが、このポリマーにより中空糸膜の内表面に平滑性を付与しているだけで中空繊維膜の内表面に水溶性ポリマーを残存させるものではない。

【００１１】特開昭61-402号、同62-38205号に開示された非対称構造を有するポリスルホン系分離膜は緻密層のみが親水化されているだけなので、分離膜を乾燥すると透水性が著しく低下する。また、親水化されていない部分での蛋白吸着が生じる。

【００１２】したがって、本発明の目的は従来のポリスルホン系分離膜の上記問題を解消した、生体適合性に優れ、かつ乾燥した後に透水性の低下のない、特に血液処理に適したポリスルホン系中空繊維膜を提供することにある。本発明の他の目的は、上記ポリスルホン系中空繊維膜の製造方法を提供することにある。

【００１３】

【課題を解決するための手段】本発明者らは上記課題を達成すべく従来のポリスルホン系中空糸膜とその製造方法について検討したところ、意外にも中空糸膜にポリグリコール類とビニルピロリドン系ポリマーを含有させ、かつ中空糸膜の内表面にビニルピロリドン系ポリマーを

多量に存在させると、ポリスルホン系ポリマーの優れた物理化学的性能と、ビニルピロリドン系ポリマーの優れた親水性の両方の性能を併せ持つ、特に抗血栓性に優れた中空繊維膜が提供できることを見出し、更に検討した結果本発明に到達したものである。

【００１４】すなわち、本発明のポリスルホン系中空繊維膜は、ポリスルホン系ポリマーからなる、内表面に緻密層をもつ非対称構造の中空繊維膜であって、該中空繊維膜はポリスルホン系ポリマーを主成分とし、少なくとも１重量%のポリグリコール類と１～８重量%のビニルピロリドン系ポリマーを含有し、かつ中空繊維膜の内表面の緻密層に存在するポリスルホン系ポリマーとビニルピロリドン系ポリマーの重量比率が90：10～60：40で、しかも中空繊維膜の内表面の上記緻密層に存在するビニルピロリドン系ポリマーの重量比率が外表面層に存在するビニルピロリドン系ポリマーの重量比率の少なくとも1.1倍であることを特徴とする。

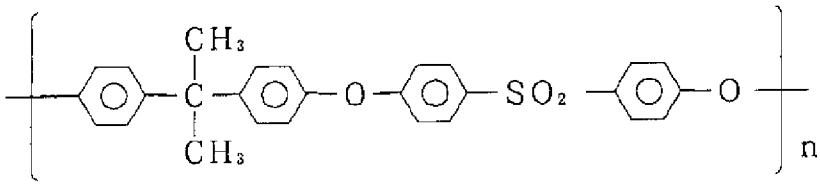
【００１５】また本発明にかかるポリスルホン系中空繊維膜の製造方法は、ポリスルホン系ポリマーと重量平均分子量が 200～ 6000のポリグリコール類および重量平均分子量が少なくとも10000のビニルピロリドン系ポリマーとを混合溶解した製膜原液を環状オリフィスより吐出させる工程と、 0.1～４重量%のビニルピロリドン系ポリマーを含有する溶液を上記吐出原液の環状の流れの内部に供給してポリスルホン系中空繊維膜を形成する工程と、該製膜されたポリスルホン系中空繊維膜を、該ポリスルホン系ポリマーに対して貧溶媒作用を有する溶液で処理して、中空繊維膜の内表面の緻密層に存在するビニルピロリドン系ポリマーの重量比率が外表面層に存在するビニルピロリドン系ポリマーの重量比率の少なくとも 1.1倍となるように調整する工程とを含んでなることを特徴とする。

【００１６】本発明のポリスルホン系中空繊維膜を製造するために用いる原液は、基本的には、ポリスルホン系ポリマー、重量平均分子量が 200～6000のポリグリコール類、重量平均分子量が少なくとも１万のビニルピロリドン系ポリマーおよびそれらポリマーの共通溶媒からなる４成分系で構成される。

【００１７】ポリスルホン系ポリマーは、通常化学式(1)または化学式 (2)で示される繰り返し単位からなるものであるが、アルキル系やスルホン基等の官能基を含んでもよい。

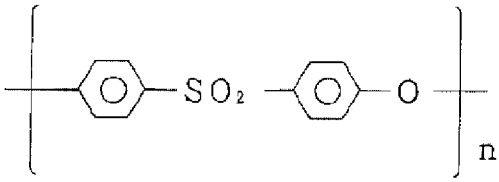
【００１８】

【化１】



【００１９】

【化２】



【００２０】原液中に含まれるポリスルホン系ポリマーの濃度は、目的用途に適合した特性を有する中空繊維膜の製造を可能とする濃度範囲であればよく、通常10～25重量%、好ましくは15～20重量%である。10重量%未満では中空繊維膜としての十分な強度を得ることができず、また実用的な中空繊維膜が形成できなくなる。また25重量%を越えると貫通孔が減少し膜の透過性能や透析性能の低下を引き起こすため実用的でない。

【００２１】ポリグリコール類は、ポリエチレングリコール、ポリプロピレングリコール、これらの共重合体、またはこれらのエステル、アミン、エーテル、アセタール誘導体で重量平均分子量が 200～6000のポリマーが用いられる。本発明では、ポリグリコール類を原液中に添加するため次のような利点がある。まずポリグリコール類の第１の作用は、ポリスルホンに対して貧溶媒の作用があるので微孔形成剤として有効で、これを添加するとミクロ相分離効果が向上して空孔率や表面開孔率の高い多孔性の膜が形成されやすくなり、優れた透過性能および透析性能を有する分離膜を得ることができる。

【００２２】第２に微孔形成剤として通常用いられている水、アルコール類、グリセリン、無機塩類等と比べて原液の増粘効果があり、しかも添加量による粘度の急激な変化がないので中空繊維膜を製造するために好適な粘性を有する原液を容易に調製することができる。

【００２３】第３に原液中にポリグリコール類を添加すると、後述するように膜内に残存させるビニルピロリドン系ポリマーの含有効率が向上する傾向が認められ、少ない添加量でも効率よくビニルピロリドン系ポリマーを中空繊維膜に含有させることができる。原液中にポリグリコール類を添加するとビニルピロリドン系ポリマーの含有効率が向上する理由は不明であるが、ポリグリコール類は他の微孔形成剤と比較して凝固の挙動が異なる、あるいは分散剤的な役割を果たす等の理由が考えられる。いずれにてしてもビニルピロリドン系ポリマーが少ない添加量でも効率よく該ビニルピロリドン系ポリマーを中空繊維膜中に含有させることができるので、コスト

面やビニルピロリドン系ポリマーの含有比率調整の点で有利である。また、ビニルピロリドン系ポリマーの添加量を少なくできるので、原液粘度を紡糸が安定な範囲に抑えやすい。

【００２４】第４に、原液中に添加したポリグリコール類は完全に除去されず若干量が膜内に残存するが、膜内にポリグリコール類とビニルピロリドン系ポリマーとを共存させることで抗血栓性が増強される傾向が認められる。

【００２５】このように、ポリグリコール類を用いることにより有利な点が多い。本発明において、上述の効果を効果的に発揮させるためには、原液中へのポリグリコール類の添加量は、ポリグリコール類の重量平均分子量、ポリスルホン系ポリマー濃度や溶媒の種類によって異なるが、ポリスルホン系ポリマーに対して50～300 重量%、通常 100～200 重量%添加することが好ましい。

【００２６】ビニルピロリドン系ポリマーは、主としてポリスルホン系中空繊維膜に残存して疎水性のポリスルホン系中空繊維膜に親水性を付与させるものであり、ポリグリコール類よりも重量平均分子量の大きいポリマー、通常重量平均分子量が少なくとも１万のポリマーが用いられる。かかるビニルピロリドン系ポリマーとしては、ポリビニルピロリドン、ビニルピロリドン・酢酸ビニル共重合体、ビニルピロリドン・ビニルアルコール共重合体、ビニルピロリドン・スチレン共重合体、ビニルピロリドン・ジメチルアミノエチルメタクリレート共重合体等やこれらの変性ポリマーが挙げられる。

【００２７】ビニルピロリドン系ポリマーは親水性効果を発揮する量を膜内に残存させる必要があるが、原液中にビニルピロリドン系ポリマーを大量に添加すると原液の粘度が急激に増加して中空繊維膜の製造が困難となったり、また、余剰のビニルピロリドン系ポリマーの抽出に時間がかかり、洗浄が不十分となりやすい。さらに中空繊維膜を乾燥させるとビニルピロリドン系ポリマーの中空繊維膜の外表面側へのマイグレーションが著しくなって中空繊維同士の膠着が発生し、中空繊維膜の取扱いやモジュール化時の障害となる。さらにビニルピロリドン系ポリマーの添加量が増加すると中空繊維膜中の含有重量比率が多くなって、ポリスルホン系ポリマーが持つ機械的強度、耐熱性、耐薬品性等の物理的及び化学的特性が損なわれるとともに、ビニルピロリドン系ポリマーの膨潤に伴う水透過性能あるいは透析性能の低下を引き起こすことになる。

【００２８】したがってビニルピロリドン系ポリマーを原液中に大量に添加することは必ずしも好ましいことではない。原液中へのビニルピロリドン系ポリマーの添加量はポリスルホン系中空繊維膜に親水性を付与する最小限の量が好ましい。ビニルピロリドン系ポリマーの添加量はポリスルホン系ポリマーに対して２～30重量%、通常５～15重量%添加される。

【００２９】溶媒は、ポリスルホン系ポリマー、ポリグリコール類、ビニルピロリドン系ポリマーを全て溶解するものであり、ジメチルホルムアミド、ジメチルアセトアミド、Ｎ－メチル－２－ピロリドン、ジメチルスルホキシド、スルホラン、ジオキサン等の多種の溶媒、あるいは上記２種類以上の混合液からなる溶媒が用いられるが、特にジメチルホルムアミド、ジメチルアセトアミドが好ましく用いられる。

【００３０】上記組成の組み合わせにより、種々の性状をもつ原液を得ることができる。例えば、溶解性の低い溶媒を用い、かつポリグリコール類の添加量を多くすると、特定の温度以上、または特定の温度以下でも相分離する原液が得られる。この原液を用いて相分離温度付近で紡糸すると精密濾過等に適した比較的ポーラスな孔を有する中空繊維膜が製造できる。逆に、溶解性の良い溶媒を用い、かつポリグリコール類の添加量を少なくすると比較的安定な原液性状となり限外濾過や透析等に適した緻密な膜が製造できる。

【００３１】以上の系からなる原液を用いてポリスルホン系中空繊維膜を得る。製膜操作は公知の乾湿式法を用いることができ、一定の温度に保温された上記原液及び内部凝固液が２重管構造の環状ノズルより同時に吐出され、凝固浴に導入される。乾湿式法では、ノズル吐出から凝固浴に浸漬する前に気体中（一般的には空気中）を通過させる。ノズルの吐出面と凝固浴表面の気中走行距離（以下ドライゾーン長という）は通常 0.1～100cm 、特に１～50cmが好ましい。 0.1cmより短いと凝固浴の僅かな波立ちでノズルが凝固浴に接触して乾湿式紡糸することが困難となる。また 100cmを越えると多ホール紡糸においては糸揺れによる中空繊維同士の膠着が発生する。ドライゾーン中を加湿させると空気中の水分によりミクロ相分離や緩和な凝固が促進され、孔径の大きな多数の微孔を有する外表面層を備えた中空繊維膜を容易に得ることができる。この効果は、ドライゾーン長が 0.1cmと非常に短くても認められ、凝固浴に直接浸漬する湿式法とは全く異なった外表面層構造を有する中空繊維膜が得られる。

【００３２】さらに原液のノズル吐出口での線速度に対する導糸速度の比（以下ノズルドラフトという）を変化させることにより膜内外表面層の微細孔の形状を変化させることもできる。ノズルドラフトを大きくすれば細長いスリット状の微細孔となりやすく、逆に小さくすれは比較的円形の微細孔となりやすい。しかし、極端にノズルドラフトを大きくしたり、また小さくすると製造が不安定となるので、ノズルドラフトは通常２～５の範囲に設定される。

【００３３】また本発明においては、中空繊維膜内表面の緻密層に存在するビニルピロリドン系ポリマーの重量比率を向上させるためにビニルピロリドン系ポリマーを含有した内部凝固液を用いる。内部凝固液に使用される

ビニルピロリドン系ポリマーは、必ずしも原液に添加したものと同一である必要はなく、種類が異なっていたり分子量の異なるものを使用してもよいが、重量平均分子量が小さいポリマーを用いると凝固時に膜内部に拡散しやすくなり、期待したほど内表面緻密層に存在する重量比率が向上しない場合がある。透析膜等の緻密な膜では重量平均分子量の小さいポリマーも使用できるが、一般的には重量平均分子量10万以上の高分子量のものを用いるほうが少ない添加量で効率よく内表面緻密層側に存在する重量比率のみを増加できるので好ましい。

【００３４】内部凝固液としては水、アルコール類、グリコール類等のポリスルホン系ポリマーに対して非溶媒または貧溶媒の単独や２種類以上の混合液にビニルピロリドン系ポリマーを添加した系が用いられる。更に、これらに溶媒を添加すると凝固速度が変化し孔径制御に役立つので好適である。溶媒を添加する場合は溶媒重量比率を10～90%、特に30～80%にすることが好ましい。10%以下は溶媒の効果が少なく、90%以上では凝固速度が非常におそくなるので紡糸が困難となる。また、塩化リチウム、塩化亜鉛、硝酸ナトリウム等の無機塩を添加すると表面開孔率が増加する等好ましい場合がある。内部凝固液に添加するビニルピロリドン系ポリマーは、通常 0.1～４重量%が好ましい。 0.1重量%以下では内表面緻密層中に存在するビニルピロリドン系ポリマーの重量比率増加の効果が不十分であり、４重量%を越えると余剰のビニルピロリドン系ポリマーの洗浄に時間がかかり経済的ではない。また、内表面緻密層中に存在するビニルピロリドン系ポリマーの重量比率が過剰となり透過性能や透析性能の低下等の問題が発生する恐れがある。したがって、添加量については、ビニルピロリドン系ポリマーの種類、重量平均分子量、原液中のビニルピロリドン系ポリマー含量等を考慮にいれて選択する必要がある。ただし、内部凝固液はビニルピロリドン系ポリマーが完全に溶解された溶液を使用する必要があり、この条件を満たす組成、濃度に設定しなければならない。

【００３５】凝固液には水、アルコール類、グリコール類等のポリスルホン系ポリマーの非溶媒、または貧溶媒の単独、あるいは２種類以上の混合液、さらにこれらと溶媒との混合液が用いられるが、ポリスルホン系ポリマーの貧溶媒または非溶媒の作用のあるもので極性溶媒、ポリグリコール類及びビニルピロリドン系ポリマーと相溶性がある溶液であれば特に制限はない。

【００３６】凝固浴で凝固した中空繊維膜は、次いで水洗または40～70℃以下の温水洗浄で溶媒、ポリグリコール類、ビニルピロリドン系ポリマーが抽出除去される。この際ポリグリコール類は大部分が、ビニルピロリドン系ポリマーは余剰分が抽出されるが、どちらも完全には抽出されず膜中に残存する。ポリグリコール類、ビニルピロリドン系ポリマーが中空繊維膜中に残存する理由としては凝固の際に膜中に取り込まれ固定化されるためと推測される。

【００３７】次に、場合によっては80℃以上の熱水処理を行う。熱水処理を予め行っておくと、溶媒、ポリグリコール類、ビニルピロリドン系ポリマーの洗浄効率が向上する上に熱に対する安定性が向上し、たとえば 100℃以上の高圧蒸気滅菌を行った際に中空繊維膜の収縮等が防止できるので有効である。

【００３８】本発明では上記工程の後、さらに中空繊維膜をポリスルホン系ポリマーに対して貧溶媒作用を有する溶液によって処理し、膜全体、特に外表面側の余剰のビニルピロリドン系ポリマーの抽出除去を行う。貧溶媒作用を有する溶媒とは、ポリスルホン系ポリマーに対して溶解はしないが膨潤等の何らかの作用を有するもので、かつビニルピロリドン系ポリマーを溶解するものをいい、アルコール類、エチレングリコール、プロピレングリコール、グリセリン、重量平均分子量 600以下のポリエチレングリコールの単独や混合液またはそれらの１重量%以上の水溶液が例示できる。また処理方法には、中空繊維膜を凝固して洗浄した後に引き続き抽出処理する方法と、膜を乾燥してモジュールを作製したのちにモジュール毎に抽出処理する方法があるが、例えば膜を乾燥させたときに中空繊維膜同士の膠着が発生しモジュール化時の障害となり得る場合は前者の方法を用い、膠着の問題はあまりなくモジュール化後の方が効率的である場合は後者の方法を用いるというように、製造条件、工程通過性、製造効率、コスト等を考慮して選択することができる。また、両方で処理することも可能である。該処理は製造安定性を向上し、さらにビニルピロリドン系ポリマーの含有量や分布状態を血液処理に適した状態に調節することを目的としているので、処理液組成や処理時間はこの点を充分考慮して設定する必要がある。

【００３９】水洗、熱水洗処理、貧溶媒作用を有する溶液での処理等を行うと余剰のポリグリコール類やビニルピロリドン系ポリマーが抽出除去され、中空繊維膜中に取り込まれ固定化されたものだけが残存するため、使用時にこれらが溶出することはほとんどない。

【００４０】本発明の中空繊維膜は、透析型人工腎臓装置承認基準に示された「透析器の品質および試験法」の透析膜の溶出物試験（以下これを人工腎臓承認基準と略称する）に記載されている方法により、溶出物の評価を行うと、紫外線吸収スペクトルとして、層長10㎜で波長 220～350nm における吸光度が 0.1以下であり、そのままの状態でも人工腎臓承認基準に合格するものである。このように、本発明の中空繊維膜は、例えば、熱処理、アルカリ加熱処理、γ線処理等の従来公知の手段によりビニルピロリドン系ポリマーを架橋構造化し、水に対して不溶化する処理を特別に行わなくても、血液処理装置、特に透析型人工腎臓に使用できる。

【００４１】これらの処理を終えた中空繊維膜は、たとえば枠等に捲き取り、乾燥される。乾燥した中空繊維膜

は束ねられ、その両端部はポリウレタンなどの熱硬化性ポリマーによりハウジングに固定されモジュール化される。該モジュールは、ＥＯＧ滅菌、高圧蒸気滅菌等の公知の方法で滅菌処理された後、体液等の処理装置として、血液透析、血液濾過、血液濃縮などに供される。

【００４２】上記製造方法により、ポリグリコール類を少なくとも１重量%、ビニルピロリドン系ポリマーを１～８重量%含有し、かつ中空繊維膜の内表面緻密層に存在するポリスルホン系ポリマーとビニルピロリドン系ポリマーの重量比率が90：10～60：40で、しかも中空繊維膜の内表面緻密層に存在するビニルピロリドン系ポリマーの重量比率が外表面層に存在するビニルピロリドン系ポリマーの重量比率の少なくとも 1.1倍である、特に血液処理用に適したポリスルホン系中空繊維膜を得ることができる。

【００４３】上記中空繊維膜中に存在するポリグリコール類の重量比率およびビニルピロリドン系ポリマーの重量比率はＮＭＲによって決定され、中空繊維膜の内表面緻密層と外表面層に存在するビニルピロリドン系ポリマーの重量比率はＸ線光電子分光法（ＥＳＣＡ）によって決定される。また、中空繊維膜の抗血栓性の良否を判断する簡単な評価方法として、血液を流通させた後のモジュールを解体し、血栓によって閉塞している中空繊維膜の数を数える方法と、血小板損傷による放出因子であるβトロンボグロブリンの濃度の増加または血液凝固系の活性によって最終段階であるフィブリノーゲンがフィブリンとなるときに生成されるフィブリノペプタイドＡの濃度の増加を測定する方法がある。

【００４４】本発明のポリスルホン系中空繊維膜は以下の理由により、ポリグリコール類とビニルピロリドン系ポリマーの両方を含む必要がある。すなわち、中空繊維膜がその内表面緻密層にビニルピロリドン系ポリマーをビニルピロリドン系ポリマーとポリスルホン系ポリマーの重量比率が15／85となるように含有し、かつポリグリコール類の含有比率が２重量%となるように紡糸したポリスルホン系中空繊維膜（Ａ）と、該中空繊維膜（Ａ）と同じ内表面緻密層における重量比率でビニルピロリドン系ポリマーを含むが、ポリグリコール類を含有しない中空繊維膜（Ｂ）を用いて、それぞれ膜面積が 1.7㎡の人工腎臓用モジュールを組み立てた後、同一の慢性腎不全患者の治療に適用した。使用後モジュールを解体し血液凝固によって閉塞した中空繊維の本数を数え閉塞率を比較すると、ポリグリコール類を含有した中空繊維膜を用いた人工腎臓（Ａ）では閉塞率が５%に過ぎないが、ポリグリコール類を含有しない中空繊維膜を用いた人工腎臓（Ｂ）では閉塞率が65%となり、ポリスルホン系中空繊維膜中にビニルピロリドン系ポリマーとポリグリコール類とを共存させることが抗血栓性に対して極めて有効であることが示された。

【００４５】更に、本発明のポリスルホン系中空繊維膜には、少なくとも１重量%のポリグリコール類が存在する必要がある。１重量%未満では抗血栓性に問題があり血液処理用に適用することができない。

【００４６】次にポリスルホン系中空繊維膜の内表面緻密層に存在するポリスルホン系ポリマーとビニルピロリドン系ポリマーの重量比率は90：10～60：40であることを要する。即ち、上記比率を種々に変えて製造したポリスルホン系中空繊維膜を用いて有効膜表面積 500 cm^2のミニモジュールを作成し、これらに新鮮な血液を流通させた。ミニモジュールを通過する血液中のβトロンボグロブリンおよびフィブリノペプタイドＡの濃度を、血液を流通させる血液回路のみのそれらの濃度（ブランク）と対比した。少なくとも１重量%のポリグリコール類を含んでなる中空繊維膜については、内表面緻密層に存在するビニルピロリドン系ポリマーとポリスルホン系ポリマーの重量比率が少なくとも10／90であれば、βトロンボグロブリンおよびフィブリノペプタイドＡの濃度はそれぞれブランク濃度の 110%以下及び 120%以下であり抗血栓性に優れるのに対し、上記ビニルピロリドン系ポリマーとポリスルホン系ポリマーの重量比率が10／90未満であれば、これら指標となる物質の濃度は、それぞれブランク濃度の 350%及び 400%にもなり、抗血栓性に劣る。血液流通後のミニモジュールを解体し、血栓によって閉塞している中空繊維膜の数を数えると、ビニルピロリドン系ポリマーとポリスルホン系ポリマーの重量比率が少なくとも10／90であれば数%程度の中空繊維膜が閉塞してしるのに対し、上記重量比率が10／90未満では50%以上の中空繊維膜の閉塞が観察された。一方、ビニルピロリドン系ポリマーとポリスルホン系ポリマーの重量比率が40／60より大であれば、βトロンボグロブリンおよびフィブリノペプタイドＡの濃度はブランク濃度の 105%～ 110%であり、抗血栓性は維持されるが、親水性ポリマーの膨潤により透水性能は小さくなる。これらの点から、中空繊維膜が少なくとも１重量%のポリグリコール類を含有する場合に、優れた抗血栓性を有するためには、血液が接触する中空繊維膜内表面の緻密層に存在するビニルピロリドン系ポリマーとポリスルホン系ポリマーのの重量比率を少なくとも10／90とする必要があり、透水性能や中分子量物質の透過性能を維持するためには内表面の緻密層に存在するビニルピロリドン系ポリマーとポリスルホン系ポリマーの重量比率を40／60以下に抑える必要がある。

【００４７】また、本発明の中空繊維膜においては、膜の内表面緻密層に存在するビニルピロリドン系ポリマーの重量比率が外表面層に存在するビニルピロリドン系ポリマーの重量比率の 1.1倍以上である。このように、ビニルピロリドン系ポリマーを中空繊維膜内表面緻密層に多量に存在させると、中空繊維膜の内外表面層に存在するビニルピロリドン系ポリマーの重量比率が同じである従来の中空繊維膜に比べ透水性が３倍以上、イヌリンの

透過率が２倍以上と透過性能を格段に向上させることができる。また本発明の中空繊維膜はアルブミンがほとんど透過しない（透過率５％以下）シャープな分画性を有し、尿素などの低分子量物質のみならず、低分子量タンパク質であるβ２－ミクログロブリンに至るまで高い透析性能を有する。透過性能や透析性能が向上する理由は、ビニルピロリドン系ポリマーを膜全体に比較的均一に含有させるよりも内表面層に多量に存在させる方が、膜全体のビニルピロリドン系ポリマーの含有量を少なくできるのでビニルピロリドン系ポリマーの膨潤による透過抵抗を小さくできるためである。なお、中空繊維膜の抗血栓性に与える影響から、膜の内表面緻密層に存在するビニルピロリドン系ポリマーの重量比率が外表面層に存在するビニルピロリドン系ポリマーの重量比率の 1.5倍以上、特に 2.0倍以上であることが好ましい。

【００４８】さらに、親水性や優れた透水性能や物質の透過性能を有するためには、中空繊維膜全体に含有されるビニルピロリドン系ポリマーは１～８重量%、通常２～５重量%が好ましい。１重量%未満では親水性が不十分であり、８重量%を越えるとビニルピロリドン系ポリマーの膨潤に伴う透過性能や透析性能の低下が起り、更にはポリスルホン系ポリマーのもつ機械的強度、耐熱性、耐薬品性等の物理的または化学的特性が失われる。

【００４９】本発明の中空繊維膜は、その内径が50～500 μｍ、膜厚が５～250 μｍ である。内径が50μｍ 未満では圧力損失が大きく、500 μｍ を越えるとモジュールが大きくなりすぎて取扱が不便である。また膜厚が５μｍ 未満では紡糸が困難でリークが発生し易く、250 μｍ を越えると透水性や透析性が著しく低下する他、モジュールが大きくなり不経済である。

【００５０】中空繊維膜の外表面層には0.05～１μｍ の微孔が多数存在し、内表面緻密層にはスリット幅0.001～0.05μｍ の多数のスリット状微孔を有している。また、断面構造は、内表面側に厚さ 0.1～３μｍ の実質的に物質を分離する緻密層を有し、膜断面中央部に向かって孔径が徐々に拡大し、中央部は平均孔径１～５μｍ の網状組織、外表面側は平均孔径 0.1～0.5 μｍ の網状組織で構成された非対称の膜構造である。

【００５１】外表面に孔の認められないような緻密層を有する中空繊維膜では、濾過速度が小さく、特に血液処理に用いた場合、濾過速度が遅くなるとともに、除去対象物質である低分子量タンパク質の透過性能や、分子量数千～１万付近の中分子量物質の透過性能も低くなり、また、尿素などの低分子量物質の透析性能も著しく低下するが、本発明のポリスルホン系中空繊維膜は内表面に緻密層、外表面に中央部よりは緻密な網状構造を有しているので、機械的強度に優れリークが発生しにくく、かつ優れた溶質透過性を保持することができる。

【００５２】

【実施例】以下実施例により本発明をさらに具体的に説明するが、本発明はこれにより何ら限定されるものではない。なお、透水性は有効長15cmの内圧型ラボモジュールを作成し、25℃、通水圧 0.5Kg/cm^{2}の条件で一定時間内に中空繊維膜を透過した水の量を測定し、算出した。

【００５３】また中空繊維膜内に存在するポリグリコール類とビニルピロリドン系ポリマーのそれぞれの重量比率は核磁気共鳴分析（ＮＭＲ）法で測定した。また、中空繊維膜の内表面緻密層または外表面層に存在するビニルピロリドン系ポリマーの重量比率は、Ｘ線光電子分光（ＥＳＣＡ）法で次のようにして求めた。すなわちポリスルホン系ポリマーの硫黄（Ｓ）とビニルピロリドン系ポリマーの窒素（Ｎ）の存在比率を求め、このＳとＮの存在比率をポリスルホン系ポリマーの重量（W_{ps}）とビニルピロリドン系ポリマーの重量（W_{vp}）にそれぞれ換算し、内表面緻密層または外表面層に存在するビニルピロリドン系ポリマーの重量比率（Ｒ%）を次式（１）により算出した。

$$R\ (\%) = W_{vp} / (W_{ps} + W_{vp}) \times 100 \quad \cdots (1)$$

【００５４】また中空繊維膜の内表面緻密層に存在するビニルピロリドン系ポリマーの重量比率（R_{in}）と外表面層に存在するビニルピロリドン系ポリマーの重量比率（R_{out}）の比（Ｐ）は次式（２）により算出した。

$$P = R_{in} / R_{out} \quad \cdots (2)$$

【００５５】実施例１

ポリスルホン（アモコ社製、ユーデルＰ1700、以下「ＰＳ」と略称する）17重量%、ポリエチレングリコール（三洋化成工業社製、ＰＥＧ 600、重量平均分子量 600、以下「ＰＥＧ」と略称する） 12.75重量%、ポリビニルピロリドン（ＧＡＦ社製、Ｋ－90、重量平均分子量 120万、以下「ＰＶＰ」と略称する）2.55%、ジメチルアセトアミド（以下、「DMA」と略称する）67.7%を混合し、加熱攪拌して均一透明な原液を調製した。この原液を45℃にて16時間静置し、脱泡した後、外径 0.5mm、内径0.25mmの環状ノズルより、内部凝固液としてＤＭＡ40重量%、ＰＶＰ 0.5重量%、水59.5重量%で構成される溶液と同時に50℃で吐出し、相対湿度80%、50℃に調整した空気中に押し出した。ドライゾーン長10cmの空中走行後、12 m/minの速度で50℃の水中に導いて凝固させた。この時のノズルドラフトは 3.2であった。次いで、60℃の温水洗浄および90℃の熱水処理、90℃の６重量%グリセリン水溶液中に５分間の浸漬処理を行った後に枠に巻き取り、乾燥して外径 280μｍ、内径 200μｍ の中空繊維膜を得た。得られた中空繊維膜の透水性能は 200 l/m^2・hr・ (kg/cm^2)、膜中にＰＶＰとＰＥＧがそれぞれ 5.5重量%、 2.0重量%存在し、内表面緻密層に存在するＰＶＰとＰＳの重量比率は23／77、また内表面緻密層中のＰＶＰの重量比率と外表面層に存在するＰＶＰの重量比率の比は 2.0であった。また、人工腎臓承認基準により溶出物の評価を行ったところ、層長10mmで波長 220nmの紫外線吸収スペクトルにおいて 0.051の吸

光度を示し、この中空繊維膜は上記基準に合格した。

【００５６】この中空繊維膜を9700本束ね有効膜面積1.7m^{2}の人工腎臓用モジュールを組み立て、該モジュールに各々エチレンオキサイドガス滅菌、高圧蒸気滅菌、γ線滅菌を施した。これら滅菌済のモジュールをそれぞれ同一の慢性腎不全患者に適用し、残血状態（中空繊維閉塞による）の比較を行ったところ、エチレンオキサイドガス滅菌および高圧蒸気滅菌を施したものでは、中空繊維閉塞による残血が殆ど無かったが、γ線滅菌を施したものでは明らかに多かった。なお、上記の中空繊維膜をクロロホルムに溶解すると、γ線滅菌処理を施したもののみ不溶解成分が存在した。かかる不溶解成分は、ＰＶＰが架橋構造化したものと考えられ、これにより残血が多く、抗血栓性が低下したものと推定される。

【００５７】実施例２

ＰＳ17重量%、ＰＥＧ20.4重量%、ＰＶＰ1.7 重量%、ＤＭＡ60.9重量%を混合し、加熱攪拌して均一透明な原液を調製した。この原液を45℃にて16時間静置し、脱泡した後、外径 0.5㎜、内径 0.25㎜ の環状ノズルより、ＤＭＡ40重量%、ＰＶＰ 0.3重量%、水59.7重量%からなる内部凝固液とともに50℃で吐出し、50℃、相対湿度80%に調整された空中に押し出し、ドライゾーン長10cmの空中走行後、12m/min の速度で50℃の水中に導いて凝固させた。この時のノズルドラフトは 3.2であった。次いで、60℃の温水洗浄及び90℃の熱水処理、90℃の６重量%グリセンリン水溶液中に５分間浸漬した後に枠に捲きとり、乾燥して外径 280μｍ 、内径 200μｍ の中空繊維膜を得た。なお、この中空繊維膜は乾燥後の膠着糸が皆無であり、安定に製造することができた。

【００５８】この膜は、図１に示す10000 倍の走査型電子顕微鏡写真（以下ＳＥＭ写真と略称する）から、中空繊維膜の外表面層には0.05～１μｍ の多数の微細孔が存在していることが確認された。また図２に示す10000 倍のＳＥＭ写真から中空繊維膜の内表面緻密層には幅0.001 ～0.03μｍ のスリット状の微細孔が多数存在していることが確認された。図３に示す1500倍の中空繊維膜の断面を示すＳＥＭ写真、図４に示す外表面側の断面を示す10000 倍のＳＥＭ写真、図５に示す中央部の断面を示す10000 倍のＳＥＭ写真および図６に示す内表面側の断面を示す10000 倍のＳＥＭ写真より、内表面側に厚さが0.2～１μｍ の緻密層が形成され、膜断面の中央部に向かって徐々に孔径が拡大し、膜の中央部は１～３μｍ の網状組織、外表面側は 0.1～0.3 μｍ の緻密な網状組織からなる層で構成された非対称構造の膜であることが確認された。得られた中空繊維膜の透水性能は 300 l/m^2・hr・(Kg/cm^2)、膜中にＰＶＰとＰＥＧがそれぞれ 3.5重量%、 2.2重量%存在し、内表面緻密層に存在するＰＶＰとＰＳの重量比率は23／77、内表面緻密層に存在するＰＶＰの重量比率と外表面層に存在するＰＶＰの重量比率の比は 2.1であった。

【００５９】実施例３

ＰＳ17重量%、ＰＥＧ34.0重量%、ＰＶＰ 0.4重量%、ＤＭＡ 48.6 重量%を混合加熱攪拌して均一透明な製膜原液を調製した。この製膜原液を45℃にて16時間静置し、脱泡した後、外径 0.5㎜、内径0.25㎜の環状ノズルより、ＤＭＡ40重量%、ポリビニルピロリドン（ＧＡＦ社製、Ｋ－120 、重量平均分子量250 万） 1.5重量%、水58.5重量%からなる内部凝固液とともに50℃で吐出し、50℃、相対湿度80%に調整した空中に押し出した。ドライゾーン長10cmの空中走行後、12m/min の速度で50℃の水中に導いて凝固させた。この時のノズルドラフトは 3.2であった。次いで、60℃の温水洗浄及び90℃の熱水処理、90℃の５重量%グリセンリン水溶液中に５分間浸漬した後、枠に捲きとり、乾燥して外径 280μｍ 、内径 200μｍ の中空繊維膜を得た。得られた中空繊維膜の透水性能は 400 l/m^2 ・hr・(Kg/cm^2)、膜中にＰＶＰとＰＥＧがそれぞれ 2.8重量%、 2.2重量%存在し、内表面緻密層に存在するＰＶＰとＰＳの重量比率は32/68 、内表面緻密層に存在するＰＶＰの重量比率と外表面層に存在するＰＶＰの重量比率の比は16.5であった。なお、この中空繊維膜は乾燥後の膠着糸が皆無であり、安定に製造することができた。

【００６０】実施例４

ＰＳ17重量%、ＰＥＧ20.4重量%、ビニルピロリドン・酢酸ビニル共重合体（ＧＡＦ社製、Ｓ６３０、以下「ＰＶＰ／ＶＡ」と略称する） 1.7重量%、ＤＭＡ60.9重量%を混合加熱攪拌して均一透明な原液を調製した。45℃にて16時間静置し、脱泡した後、外径 0.5㎜、内径0.25㎜の環状ノズルより、ＤＭＡ40重量%、ＰＶＰ／ＶＡ 0.5重量%、水59.5重量%からなる内部凝固液とともに50℃で吐出し、50℃、相対湿度80%に調整した空中に押し出した。ドライゾーン長10cmの空中走行後、12m/min の速度で50℃の水中に導いて凝固させた。この時のノズルドラフトは 3.2であった。次いで、60℃の温水洗浄及び90℃の熱水処理、30℃の10重量%エタノール水溶液中に５分間浸漬した後に枠に捲きとり、乾燥して外径 280μｍ 、内径 200μｍの中空繊維膜を得た。得られた中空繊維膜の透水性能は 480 l/m^2 ・hr・(Kg/cm^2)、膜中にＰＶＰ／ＶＡとＰＥＧがそれぞれ 3.2重量%、 2.1重量%存在し、内表面緻密層に存在するＰＶＰ／ＶＡとＰＳの重量比率は21/79 、内表面緻密層に存在するＰＶＰ／ＶＡの重量比率と外表面層に存在するＰＶＰ／ＶＡの重量比率の比は 1.7であった。なお、この中空繊維膜は乾燥後の膠着糸が皆無であり、安定に製造することができた。

【００６１】実施例５

ＰＳ17重量%、ＰＥＧ10.2重量%、ＰＶＰ 1.7重量%、ＤＭＡ71.1重量%を混合加熱攪拌して均一透明な原液を調製した。45℃にて16時間静置し、脱泡した後、外径 0.5㎜、内径0.25㎜の環状ノズルより、ＤＭＡ40重量

%、ＰＶＰ 0.5重量%、水59.5重量%からなる内部凝固液とともに50℃で吐出し、50℃、相対湿度80%に調整された空中に押し出した。ドライゾーン長10cmの空中走行後、12m/minの速度で50℃の水中に導いて凝固させた。この時のノズルドラフトは 3.2であった。次いで、60℃の温水洗浄及び90℃の熱水処理、80℃の８重量%グリセリン水溶液中に10分間浸漬した後に枠に巻きとり、乾燥して外径 280μｍ 、内径 200μｍの中空繊維膜を得た。得られた中空繊維膜の透水性能は 260 l/m^2 ・hr・(Kg/cm^2)、膜中にＰＶＰとＰＥＧがそれぞれ 2.8重量%、1.9重量%存在し、内表面緻密層に存在するＰＶＰとＰＳの重量比率は15/85 、内表面緻密層に存在するＰＶＰの重量比率と外表面層に存在するＰＶＰの重量比率の比は 1.9であった。なお、この中空繊維膜は乾燥後の膠着糸が皆無であり、安定に製造することができた。

【００６２】比較例１

ＰＳ17重量%、ＰＥＧ34.0重量%、ＤＭＡ49.0重量%を混合加熱攪拌して均一透明な原液を調製した。45℃にて16時間静置し、脱泡した後、外径 0.5㎜、内径0.25㎜の環状ノズルより、ＤＭＡ40重量%、水60重量%からなる内部凝固液とともに50℃で吐出し、50℃、相対湿度80%に調整された空中に押し出した。ドライゾーン長10cmの空中走行後、12m/min の速度で50℃の水中に導いて凝固させた。この時のノズルドラフトは 3.2であった。次いで、60℃の温水洗浄及び90℃の熱水処理を行った後に、90℃のグリセリン10重量%水溶液に15分間膜を浸漬した後に枠に巻きとり、乾燥して外径 280μｍ、内径 200μｍの中空繊維膜を得た。得られた中空繊維膜の透水性能は 800 l/m^2 ・hr・(Kg/cm^2)であった。

【００６３】比較例２

ＰＳ17重量%、水 1.0重量%、ＰＶＰを 6.0重量%、ＤＭＡ76.0重量%を混合加熱攪拌して均一透明な原液を調製した。45℃にて16時間静置し、脱泡した後、外径 0.5㎜、内径0.25㎜の環状ノズルより、ＤＭＡ40重量%、水60重量%からなる内部凝固液とともに50℃で吐出し、50℃、相対湿度80%に調整された空中に押し出した。ドライゾーン長10cmの空中走行後、12m/min の速度で50℃の水中に導いて凝固させた。この時のノズルドラフトは 3.2であった。次いで、60℃の温水洗浄及び90℃の熱水処理、80℃の８重量%グリセリン水溶液中に10分間浸漬した後に枠に巻きとり、乾燥して外径 280μｍ 、内径 200μｍの中空繊維膜を得た。得られた中空繊維膜の透水性能は 80 l/m^2・hr・(Kg/cm^2)、膜中にＰＶＰが５重量%存在し、内表面緻密層に存在するＰＶＰとＰＳの重量比率は16／84、内表面緻密層に存在するＰＶＰの重量比率と外表面層に存在するＰＶＰの重量比率の比は 0.7であった。なお、この中空繊維膜は乾燥後の膠着糸が非常に多く、安定に製造することができなかった。

【００６４】比較例３

実施例２の原液を用い、ＤＭＡ40重量%、水60重量%からなる内部凝固液とともに50℃で吐出し、50℃、相対湿度80%に調整された空中に押し出した。ドライゾーン長10cmの空中走行後、12m/min の速度で50℃の水中に導いて凝固させた。この時のノズルドラフトは 3.2であった。次いで、60℃の温水洗浄及び90℃の熱水処理、90℃の６重量%グリセリン水溶液中に５分間浸漬した後に枠に巻きとり、乾燥して外径 280μｍ 、内径 200μｍの中空繊維膜を得た。得られた中空繊維膜の透水性能は600 l/m^2・hr・(Kg/cm^2)、膜中にＰＶＰとＰＥＧがそれぞれ 3.0重量%、 2.1重量%存在し、内表面緻密層に存在するＰＶＰとＰＳの重量比率は 8／92、内表面緻密層に存在するＰＶＰの重量比率と外表面層に存在するＰＶＰの重量比率の比は 0.8であった。

【００６５】比較例４

実施例２の方法で得られた中空繊維膜を60℃の温水洗浄し、90℃の熱水処理を行った後、グリセリン水溶液中へ浸漬することなく、枠に巻きとり、乾燥して外径 280μｍ 、内径 200μｍ の中空繊維膜を得たが、乾燥後の中空繊維膜同士の膠着が多く、安定に製造することができなかった。また得られた中空繊維膜の透水性能は 125 l/m^2 ・hr・(Kg/cm^2)と極めて低く実用上問題がある。

【００６６】実施例６

ＰＳ17重量%、ＰＥＧ22.0重量%、ＰＶＰ 1.7重量%、ジメチルホルムアミド59.3重量%を混合加熱攪拌して均一透明な原液を調製した。45℃にて16時間静置し、脱泡した後、外径 0.7㎜、内径 0.3㎜の環状ノズルより、ジメチルホルムアミド59.5重量%、ＰＶＰ 0.5重量%、水40重量%からなる内部凝固液とともに30℃で吐出し、相対湿度80%、50℃に調整された空中に押し出した。ドライゾーン長10cmの空中走行後、10.5m/min の速度で50℃の水中に導いて凝固させた。この時のノズルドラフトは 3.8であった。次いで、60℃の温水洗浄及び90℃の熱水処理、75℃の 7.5重量%グリセリン水溶液中に10分間浸漬した後に枠に巻きとり、乾燥して外径 360μｍ 、内径 230μｍ の中空繊維膜を得た。得られた中空繊維膜の透水性能は850 l/m^2・hr・(Kg/cm^2)、膜中にＰＶＰとＰＥＧがそれぞれ 2.7重量%、 1.8重量%存在し、内表面緻密層に存在するＰＶＰとＰＳの重量比率は20／80、内表面緻密層に存在するＰＶＰの重量比率と外表面層に存在するＰＶＰの重量比率の比は 3.0であった。なお、この中空繊維膜は乾燥後の膠着糸が皆無であり、安定に製造することができた。

【００６７】実施例７

実施例２、３、５と比較例１～３で得られた中空繊維膜を9700本束ね有効膜面積 1.7m^{2}の人工腎臓用モジュールを組み立てた。これらはすべてウェット状態で高圧蒸気滅菌を行った。該モジュールを用いて、ＵＦＲ（限外濾過速度）および透析性能を日本人工臓器学会の性能評価基準に基づいて測定した。またアルブミン、イヌリンのふるい係数の測定は、ハイパフォーマンスメンブレン研

究会に示された方法（腎と透析　別冊 27 167 (1989)）で行った。測定結果を表１に示す。表１から、実施例２、３、５は透析性能等すべてに優れ、しかも残血（中空繊維の閉塞による）が少なく抗血栓性に優れていた。一方比較例１は透析性能等すべてに優れているが、抗血栓性に問題がある。また比較例２、３は透析性能が低く、かつ抗血栓性にも問題があった。

【００６８】

【表１】

	C urea. (ml/min)	C inu. (ml/min)	S c Alb.	S c inu.	UFR 注1	残血状態 注2
実施例２	190	103	0.001	0.99	6.4	◎
実施例３	191	110	0.001	0.99	9.1	◎
実施例５	185	98	0.001	0.97	5.1	○
比較例１	195	128	0.002	0.99	17.5	×
比較例２	158	57	0.000	0.48	2.3	△
比較例３	192	89	0.000	0.95	12.1	×

【００６９】

urea; 尿素、inu.イヌリン、Alb;アルブミン

注１）　単位：ml/(min ・m^2・mmHg)

注２）　残血：◎；殆ど無、○；少　△；やや多い　×；多

【００７０】

【発明の効果】以上のように、本発明のポリスルホン中空繊維膜は、特に生体適合性、延いては抗血栓性に優れるような親水性高分子の種類、含有量、存在形態を有し、さらに高い透水性、シャープな分画性を有しているので、本発明のポリスルホン系中空繊維膜を使用して体液処理を行うと、例えば、血液透析においては、優れた抗血栓性の効果により残血（中空繊維の閉塞による）がない、または非常に少ないので安全に透析治療が実施できる。また、持続的血液濾過（ＣＡＶＨ）のように長時間連続的に濾過を行う治療においては、少量のヘパリン投与で、血栓による中空繊維膜の閉塞がなく長時間安定して治療に用いることができ、さらに、中分子量物質は透過されるが、有用タンパク質であるアルブミンはほとんど除去されないので、血液の膠質浸透圧が維持可能である。また本発明によるポリスルホン系中空繊維膜の製造方法は、原液の粘度調整が容易で、かつ中空繊維膜の外表面層に存在するビニルピロリドン系ポリマーの重量比率が低いため、中空繊維膜の製造工程において、中空繊維膜同士の膠着がなく安定に中空繊維膜を製造できる。

【図面の簡単な説明】

【図１】実施例２で得られたポリスルホン系中空繊維膜の外表面層の構造を示す10000倍のＳＥＭ写真である。

【図２】上記中空繊維膜の内表面緻密層の構造を示す10000 倍のＳＥＭ写真である。

【図３】上記中空繊維膜の断面構造を示す1500倍のＳＥＭ写真である。

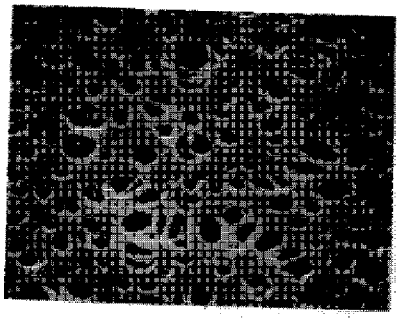
【図４】上記中空繊維膜の外表面側の断面構造を示す10000 倍のＳＥＭ写真である。

【図５】上記中空繊維膜の中央部の断面構造を示す10000 倍のＳＥＭ写真である。

【図６】上記中空繊維膜の内表面側の断面構造を示す10000 倍のＳＥＭ写真である。

【図１】

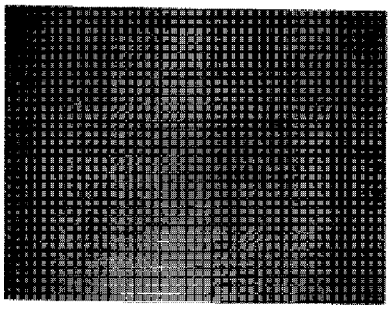
図面代用写真



（写真）

【図２】

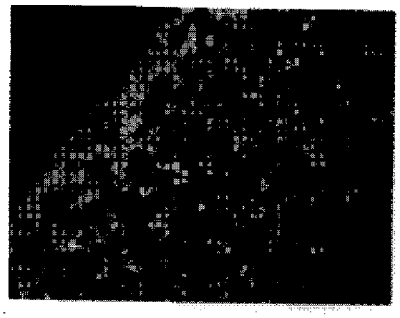
図面代用写真



（写真）

【図４】

図面代用写真



（写真）

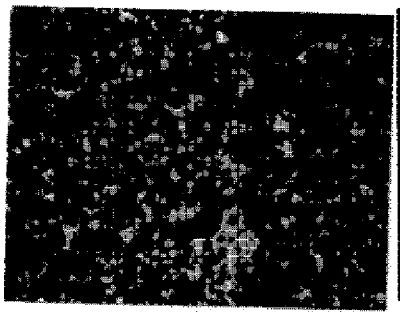
【図３】

図面代用写真

（写真）

【図５】

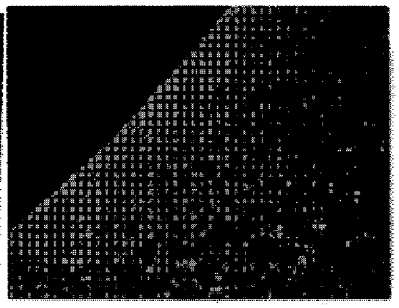
図面代用写真



（写真）

【図６】

図面代用写真



（写真）

フロントページの続き

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(54) POLYSULFONE HOLLOW FABRIC MEMBRANE AND PRODUCTION THEREFOR

(57)Abstract:
PURPOSE: To provide a polysulfone hollow fabric membrane superior in suitability for the living body, having degradation of water permeability after drying and being especially suitable for a blood treatment and the manufacturing method.
CONSTITUTION: The membrane is the hollow fabric membrane consisting of a polysulfone polymer and having an asymmetric structure having a dense layer at the inside surface, and the hollow fabric membrane incorporates ≥1wt.% a polyglycol group and 1-8wt.% a vinyl pyrrolidone polymer, and also the weight ratio of the polysulfone polymer present on the dense layer of the inside surface of the hollow fabric membrane to the vinyl-pyrrolidone polymer is (90:10)-(60:40) and the weight ratio of the vinyl pyrrolidone polymer present on the dense layer of the inside layer of the hollow fabric membrane is at least 1.1 times the weight ratio of the vinyl pyrrolidone polymer present on the outside surface layer.

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CLAIMS

[Claim(s)]
[Claim 1] It is the hollow fiber film of the unsymmetrical structure which has a compact layer in an internal surface which consists of a polysulfone system polymer. This hollow fiber film uses a polysulfone system polymer as a principal component, and contains at least 1% of the weight of polyglycols, and 1 - 8% of the weight of a vinyl-pyrrolidone system polymer. The weight ratio of a polysulfone system polymer and a vinyl-pyrrolidone system polymer which exists in the compact layer of the internal surface of the hollow fiber film and by 90:10-60:40 And it is even if there are few weight ratios of the vinyl-pyrrolidone system polymer to which the weight ratio of the vinyl-pyrrolidone system polymer which exists in the above-mentioned compact layer of the internal surface of the hollow fiber film exists in an outside-surface layer. Polysulfone system hollow fiber film characterized by being 1.1 times.
[Claim 2] Polysulfone system hollow fiber film according to claim 1 whose above-mentioned polyglycols are polyethylene glycols.
[Claim 3] Polysulfone system hollow fiber film according to claim 1 or 2 chosen from the group which the above-mentioned vinyl-pyrrolidone system polymer becomes from a polyvinyl pyrrolidone, vinyl pyrrolidone and a vinyl acetate copolymer, a vinyl-pyrrolidone vinyl alcohol copolymer, a vinyl-pyrrolidone styrene copolymer, vinyl-pyrrolidone dimethylaminoethyl methacrylate copolymers, and these denaturation polymers.
[Claim 4] Even if there are few weight ratios of the vinyl-pyrrolidone system polymer to which the weight ratio of the vinyl-pyrrolidone system polymer which exists in the compact layer of the internal surface of the hollow fiber film exists in an outside-surface layer Polysulfone system hollow fiber film given in claim 1 thru/or any of 3 they are. [which is 1.5 times]
[Claim 5] Even if there are few weight ratios of the vinyl-pyrrolidone system polymer to which the weight ratio of the vinyl-pyrrolidone system polymer which exists in the compact layer of the internal surface of the hollow fiber film exists in an outside-surface layer Polysulfone system hollow fiber film given in claim 1 thru/or any of 4 they are. [which is 2.0 times]
[Claim 6] A polysulfone system polymer and weight average molecular weight The process which makes the film production undiluted solution with which the polyglycols and weight average molecular weight of 200-6,000 carried out the mixed dissolution of the vinyl-pyrrolidone system polymer of at least 10,000 breathe out from an annular orifice, The process which supplies the solution containing 0.1 - 4% of the weight of a vinyl-pyrrolidone system polymer to the interior of the annular flow of the above-mentioned regurgitation undiluted solution, and forms the polysulfone system hollow fiber film, The produced this polysulfone system hollow fiber film is processed with the solution which has a poor solvent operation to this polysulfone system polymer. Even if there are few weight ratios of the vinyl-pyrrolidone system polymer to which the weight ratio of the vinyl-pyrrolidone system polymer which exists in the

compact layer of the internal surface of the hollow fiber film exists in an outside-surface layer The manufacture approach of the polysulfone system hollow fiber film characterized by coming to contain the process adjusted so that it may become 1.1 times.
[Claim 7] The manufacture approach of the polysulfone system hollow fiber film according to claim 6 that the above-mentioned polyglycols are polyethylene glycols.
[Claim 8] The manufacture approach of the polysulfone system hollow fiber film according to claim 6 or 7 chosen from the group which the above-mentioned vinyl-pyrrolidone system polymer becomes from a polyvinyl pyrrolidone, vinyl pyrrolidone and a vinyl acetate copolymer, a vinyl-pyrrolidone vinyl alcohol copolymer, a vinyl-pyrrolidone styrene copolymer, vinyl-pyrrolidone dimethylaminoethyl methacrylate copolymers, and these denaturation polymers.
[Claim 9] The solution which has a poor solvent operation to the above-mentioned polysulfone system polymer is water, alcohols, ethylene glycol, propylene glycol, a glycerol, and weight average molecular weight. The manufacture approach of the polysulfone system hollow fiber film given in claim 6 thru/or any of 9 they are. [which is at least one sort of liquids chosen from the group which consists of 600 or less polyethylene glycol]
[Claim 10] Even if there are few weight ratios of the vinyl-pyrrolidone system polymer to which the weight ratio of the vinyl-pyrrolidone system polymer which exists in the compact layer of the internal surface of the hollow fiber film exists in an outside-surface layer The manufacture approach of claim 6 which processes and adjusts the polysulfone system hollow fiber film with the solution which has a poor solvent operation to this polysulfone system polymer so that it may become 1.5 times thru/or the polysulfone system hollow fiber film given in 9.
[Claim 11] The manufacture approach of claim 6 which processes and adjusts the polysulfone system hollow fiber film with the solution which has a poor solvent operation to this polysulfone system polymer so that the weight ratio of the vinyl-pyrrolidone system polymer which exists in the compact layer of the internal surface of the hollow fiber film may become twice [at least] the weight ratio of the vinyl-pyrrolidone system polymer which exists in an outside-surface layer thru/or the polysulfone system hollow fiber film given in 10.

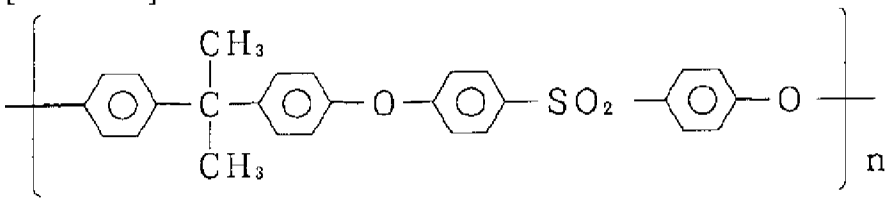
DETAILED DESCRIPTION

[Detailed Description of the Invention]
[0001]
[Industrial Application] This invention relates to the polysulfone system hollow fiber film suitable for the blood processing which made the vinyl-pyrrolidone system polymer exist in the compact layer of the internal surface of the polysulfone system hollow fiber film and its manufacture approach, especially the hollow fiber film so much, and its manufacture approach.
[0002]
[Description of the Prior Art] In recent years, the ultrafiltration method which is the separation technology using a permselectivity demarcation membrane, reverse osmosis, a gas separation method, etc. are put in practical use in various kinds of fields, and Kamiichi of the demarcation membrane made from the material which fits the various applications respectively is carried out. As a material of a permselectivity demarcation membrane, polymers, such as a cellulose system, a cellulose acetate system, a polyamide system, a polyacrylonitrile system, a polyvinyl alcohol system, a polymethylmethacrylate system, a polysulfone system, and a polyolefine system, are used. Since physicochemical qualities, such as thermal resistance, acid resistance, alkali

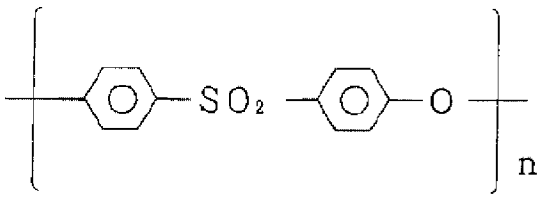
resistance, and oxidation resistance, are excellent especially, the polysulfone system polymer attracts attention as a material of medical application and an industrial use demarcation membrane also especially recently.
[0003] However, since a polysulfone system polymer is a hydrophobic material, if the permselectivity demarcation membrane made from this is bad and water wettability dries it compared with the permselectivity demarcation membrane made from the hydrophilic polymer, the engine performance will fall. Then, the examination for giving a hydrophilic property to the permselectivity demarcation membrane which consists of a polysulfone system polymer, and raising water wettability is made, and the permselectivity demarcation membrane which made the demarcation membrane which consists of hydrophobic polymers, such as a polysulfone system polymer, contain hydrophilic polymers, such as a polyvinyl pyrrolidone, and its process are proposed as the one approach.
[0004] For example, the polysulfone system demarcation membrane which was manufactured by carrying out spinning of the undiluted solution which consists of polysulfone, with a molecular weight of 100,000 or more polyvinyl pyrrolidones, and those common solvents to JP,2-18695,B and which is made to contain a with a molecular weight of 100,000 or more polyvinyl pyrrolidone five to 70% of the weight in a demarcation membrane, and has 11% or more of water-absorption-power force, and its process are indicated. The hollow fiber film for [which is made to contain a hydrophilic polymer one to 10% of the weight, and has 3 - 10% of water-absorption-power force] blood processing manufactured by carrying out spinning of the undiluted solution of hypoviscosity which consists of a hydrophobic polymer, hydrophilic polymers, and those common solvents to JP,61-93801,A, and its process are indicated.
[0005] JP,61-238306,A and 63-97666 -- a polysulfone system polymer, a hydrophilic polymer, and this polysulfone system polymer -- receiving -- a non-solvent -- or -- a swelling agent -- the manufacture approach of the polysulfone system demarcation membrane using the system which added the additive as a film production undiluted solution is indicated. Moreover, the method of insolubilizing a hydrophilic polymer is indicated by JP,63-97205,A and 63-97634 by performing radiation treatment and/or heat treatment to the polysulfone system demarcation membrane manufactured by the above-mentioned approach. In case spinning is furthermore carried out to JP,63-99325,A using the above-mentioned film production undiluted solution, the polysulfone system hollow fiber which smoothed the internal surface using the infusion which contains a water-soluble polymer at least 5% of the weight is indicated.
[0006] The average aperture obtained by JP,61-238834,A and 63-99325 according to the above-mentioned manufacturing method is 500. The polysulfone system porosity film whose amounts of water penetration which have the pore more than angstrom and contain a hydrophilic polymer three to 30% of the weight are more than 1000 ml/m2 and hr-mmHg is indicated. The demarcation membrane which only the compact layer side of the demarcation membrane which becomes JP,61-402,A and 62-38205 from the hydrophobic polymer which has unsymmetrical structure becomes from the mixture of this hydrophobic polymer and a hydrophilic polymer is indicated.
[0007]
[Problem(s) to be Solved by the Invention] By making a hydrophilic polymer exist in the film, the above-mentioned polysulfone system demarcation membrane gives water wettability to a hydrophobic polysulfone system demarcation membrane, and raises permeable ability, and moreover, although it has the outstanding engine performance -- contamination of the film by protein adsorption etc. is prevented -- sufficient examination about biocompatibility is not made

and it is not necessarily satisfied in respect of anti-thrombus nature.
[0008] For example, the polysulfone system hollow fiber film suitable for blood processing is indicated by JP,61-93801,A. although a detail in the letter has the publication of the purport which is the film which can suppress complement activity low about this hollow fiber film, the property that complement activity is suppressed low is a property discovered only when the hollow fiber film is hydrophobicity. That is, hydrophilization of the internal surface which blood contacts was not fully carried out, but the hollow fiber film indicated by JP,61-93801,A has suggested that hydrophobicity still remains. When hydrophobicity remains in the front face on which blood contacts, it is in the condition that a platelet tends to adhere. Once a platelet adheres to the internal surface of the hollow fiber film, the matter which activates a blood coagulation system by condensation of a platelet and collapse will be emitted, and blood coagulation will arise.
[0009] Moreover, since the polysulfone system demarcation membrane indicated by JP,2-18695,B has 11% or more of water absorption power, it absorbs the moisture in air during the preservation after film production. Therefore, a facility special for demarcation membrane preservation is needed. Moreover, since that water absorption power is high has much abundance of the polyvinyl pyrrolidone in a demarcation membrane, the mechanical engine performance of a demarcation membrane falls and permeable ability also falls.
[0010] Since the polysulfone system demarcation membrane indicated by a process or JP,61-238834,A of a polysulfone system demarcation membrane furthermore indicated by JP,61-238306,A, JP,63-99325,A, etc. has added the hydrophilic polymer to the film production undiluted solution, it cannot fully carry out hydrophilization of the internal surface of a demarcation membrane like the polysulfone system hollow fiber film indicated by JP,61-93801,A. Moreover, this process Although it is suitable for the process of the demarcation membrane which has a big hole 500A or more, it is not suitable for the process of the demarcation membrane for hemodialysis. Although the process of the polysulfone system demarcation membrane indicated by JP,63-99325,A is making the water-soluble polymer contain in internal coagulation liquid, a water-soluble polymer is not made to remain in the internal surface of the hollow fiber film only by this polymer having given smooth nature to the internal surface of a hollow fiber.
[0011] Since hydrophilization only of the compact layer is only carried out, if the polysulfone system demarcation membrane which has the unsymmetrical structure indicated by JP,61-402,A and 62-38205 dries a demarcation membrane, water permeability will fall remarkably. Moreover, protein adsorption in the part by which hydrophilization is not carried out arises.
[0012] Therefore, the purpose of this invention is excellent in the biocompatibility which solved the above-mentioned problem of the conventional polysulfone system demarcation membrane, and it is in offering the polysulfone system hollow fiber film suitable for especially blood processing without a permeable fall, after drying. Other purposes of this invention are to offer the manufacture approach of the above-mentioned polysulfone system hollow fiber film.
[0013]
[Means for Solving the Problem] The place which examined a conventional polysulfone system hollow fiber and its conventional manufacture approach that this invention persons should attain the above-mentioned technical problem, If a hollow fiber is made to contain polyglycols and a vinyl-pyrrolidone system polymer also unexpectedly and a vinyl-pyrrolidone system polymer is made to exist in the internal surface of a hollow fiber so much This invention is reached [that the hollow fiber film having the physicochemical engine performance which was excellent in the

polysulfone system polymer, and the engine performance of both hydrophilic properties which was excellent in the vinyl-pyrrolidone system polymer excellent in especially anti-thrombus nature can be offered, and] as a result of inquiring further, a header and.
[0014] Namely, the polysulfone system hollow fiber film of this invention It is the hollow fiber film of the unsymmetrical structure which has a compact layer in an internal surface which consists of a polysulfone system polymer. This hollow fiber film uses a polysulfone system polymer as a principal component, and contains at least 1% of the weight of polyglycols, and 1 - 8% of the weight of a vinyl-pyrrolidone system polymer. The weight ratio of a polysulfone system polymer and a vinyl-pyrrolidone system polymer which exists in the compact layer of the internal surface of the hollow fiber film and by 90:10-60:40 And it is even if there are few weight ratios of the vinyl-pyrrolidone system polymer to which the weight ratio of the vinyl-pyrrolidone system polymer which exists in the above-mentioned compact layer of the internal surface of the hollow fiber film exists in an outside-surface layer. It is characterized by being 1.1 times.
[0015] Moreover, the manufacture approach of the polysulfone system hollow fiber film concerning this invention A polysulfone system polymer and weight average molecular weight The process which makes the film production undiluted solution with which the polyglycols and weight average molecular weight of 200-6000 carried out the mixed dissolution of the vinyl-pyrrolidone system polymer of at least 10000 breathe out from an annular orifice, The process which supplies the solution containing 0.1 - 4% of the weight of a vinyl-pyrrolidone system polymer to the interior of the annular flow of the above-mentioned regurgitation undiluted solution, and forms the polysulfone system hollow fiber film, The produced this polysulfone system hollow fiber film is processed with the solution which has a poor solvent operation to this polysulfone system polymer. Even if there are few weight ratios of the vinyl-pyrrolidone system polymer to which the weight ratio of the vinyl-pyrrolidone system polymer which exists in the compact layer of the internal surface of the hollow fiber film exists in an outside-surface layer It is characterized by coming to contain the process adjusted so that it may become 1.1 times.
[0016] Fundamentally, a polysulfone system polymer and weight average molecular weight the undiluted solution used in order to manufacture the polysulfone system hollow fiber film of this invention It consists of 4 component systems which the polyglycols of 200-6000 and weight average molecular weight become from the common solvent of the vinyl-pyrrolidone system polymer of at least 10,000, and these polymers.
[0017] Although a polysulfone system polymer consists of a repeat unit usually shown with a chemical formula (1) or a chemical formula (2), it may also contain functional groups, such as an alkyl system and a sulfone radical.
[0018]
[Formula 1]



[0019]
[Formula 2]



[0020] The concentration of the polysulfone system polymer contained in an undiluted solution is usually 15 - 20 % of the weight preferably ten to 25% of the weight that what is necessary is just the density range which enables manufacture of the hollow fiber film which has the property which suited the purpose application. It becomes impossible to obtain sufficient reinforcement as hollow fiber film, and to form the practical hollow fiber film at less than 10 % of the weight. Moreover, it is not practical in order for a through tube to decrease and to cause membranous penetrable ability and dialysis performance degradation, if 25 % of the weight is exceeded.
[0021] Weight average molecular weight polyglycols with a polyethylene glycol, polypropylene glycols, these copolymers or these ester, an amine, the ether, and an acetal derivative The polymer of 200-6000 is used. In this invention, in order to add polyglycols in an undiluted solution, there are the following advantages. since an operation of the 1st of polyglycols has an operation of a poor solvent to polysulfone first -- a fine hole -- if it is effective as a formation agent and this is added, the microfacies separation effectiveness will improve and the porous film with high void content and surface hole density will form -- having -- being easy -- the demarcation membrane which has the outstanding penetrable ability and the outstanding dialysis engine performance can be obtained.
[0022] the 2nd -- a fine hole -- there is the thickening effectiveness of an undiluted solution compared with the water usually used as a formation agent, alcohols, a glycerol, mineral, etc., and since there is moreover no abrupt change of the viscosity by the addition, in order to manufacture the hollow fiber film, the undiluted solution which has suitable viscosity can be prepared easily.
[0023] If polyglycols are added in an undiluted solution to the 3rd, the inclination for the content effectiveness of the vinyl-pyrrolidone system polymer made to remain in the film to improve is accepted so that it may mention later, and the hollow fiber film can be made to contain a vinyl-pyrrolidone system polymer efficiently also with a small addition. although the reason whose content effectiveness of a vinyl-pyrrolidone system polymer improves is unknown if polyglycols are added in an undiluted solution -- the fine hole of others [polyglycols] -- the behavior of coagulation differs as compared with a formation agent, or the reasons of playing the role like a dispersant can be considered. Since a vinyl-pyrrolidone system polymer can make this vinyl-pyrrolidone system polymer contain in the hollow fiber film efficiently also with a small addition even if it carries out in any, it is advantageous in respect of content ratio adjustment of a cost side or a vinyl-pyrrolidone system polymer. Moreover, since the addition of a vinyl-pyrrolidone system polymer can be lessened, it is easy to hold down undiluted solution viscosity to the range where spinning is stable.
[0024] Although the polyglycols added in the undiluted solution to the 4th are not removed completely but an amount remains in the film a little, the inclination for anti-thrombus nature to be reinforced by making polyglycols and a vinyl-pyrrolidone system polymer live together in the film is accepted.
[0025] Thus, there are many advantageous points by using polyglycols. Although the addition of the polyglycols to the inside of an undiluted solution changes in this invention with classes of the

weight average molecular weight of polyglycols, polysulfone system polymer concentration, or solvent in order to demonstrate above-mentioned effectiveness effectively, it is 50-300 to a polysulfone system polymer. Weight %, usual 100-200 It is desirable to do weight % addition of.
[0026] A vinyl-pyrrolidone system polymer remains mainly on the polysulfone system hollow fiber film, a hydrophilic property is made to give the hydrophobic polysulfone system hollow fiber film, and the polymer of at least 10,000 is used for a polymer with larger weight average molecular weight than polyglycols, and usual weight average molecular weight. As this vinyl-pyrrolidone system polymer, a polyvinyl pyrrolidone, vinyl pyrrolidone and a vinyl acetate copolymer, a vinyl-pyrrolidone vinyl alcohol copolymer, a vinyl-pyrrolidone styrene copolymer, vinyl-pyrrolidone dimethylaminoethyl methacrylate copolymers, etc. and these denaturation polymers are mentioned.
[0027] Although it is necessary to make the amount which demonstrates hydrophilic effectiveness remain in the film, if a vinyl-pyrrolidone system polymer is added in large quantities in an undiluted solution, the viscosity of an undiluted solution increases rapidly, manufacture of the hollow fiber film will become difficult, and a vinyl-pyrrolidone system polymer will require time amount for the extract of an excessive vinyl-pyrrolidone system polymer, and it will be easy to become inadequate washing it. If the hollow fiber film is furthermore dried, the migration by the side of the outside surface of the hollow fiber film of a vinyl-pyrrolidone system polymer becomes remarkable, and conglutination of hollow fibers will occur and it will become a failure at the time of handling and modularization of the hollow fiber film. If the addition of a vinyl-pyrrolidone system polymer furthermore increases, the content weight ratio in the hollow fiber film will increase, and physical and the water permeability ability accompanying [while chemical property is spoiled] the swelling of a vinyl-pyrrolidone system polymer, or dialysis performance degradation, such as the mechanical strength and thermal resistance which a polysulfone system polymer has, and chemical resistance, will be caused.
[0028] Therefore, it is not necessarily desirable to add a vinyl-pyrrolidone system polymer in large quantities in an undiluted solution. The minimum amount of the addition of the vinyl-pyrrolidone system polymer to the inside of an undiluted solution which gives a hydrophilic property to the polysulfone system hollow fiber film is desirable. The addition of a vinyl-pyrrolidone system polymer is usually added five to 15% of the weight two to 30% of the weight to a polysulfone system polymer.
[0029] A solvent dissolves all of a polysulfone system polymer, polyglycols, and a vinyl-pyrrolidone system polymer, and although the solvent of varieties, such as dimethylformamide, dimethylacetamide, a N-methyl-2-pyrrolidone, dimethyl sulfoxide, a sulfolane, and dioxane, or the solvent which consists of the two or more above-mentioned kinds of mixed liquor is used, especially dimethylformamide and dimethylacetamide are used preferably.
[0030] An undiluted solution with various descriptions can be obtained with the combination of the above-mentioned presentation. For example, if the addition of polyglycols is made [many], using a soluble low solvent, the undiluted solution which carries out phase separation of beyond specific temperature or below specific temperature will be obtained. If spinning is carried out near phase separation temperature using this undiluted solution, the hollow fiber film which has a comparatively porous hole suitable for precision filtration etc. can be manufactured. On the contrary, using a soluble good solvent, if the addition of polyglycols is lessened, the precise film which became the shape of comparatively stable Hara acidity or alkalinity, and fitted an ultrafiltration, dialysis, etc. can be manufactured.
[0031] The polysulfone system hollow fiber film is obtained using the undiluted solution which

consists of the above system. Film production actuation can use a well-known dryness-and-moisture type method, and the above-mentioned undiluted solution and internal coagulation liquid which were kept warm by fixed temperature are breathed out by coincidence from the annular nozzle of double tubing structure, and it is introduced into a coagulation bath. By the dryness-and-moisture type method, before being immersed in a coagulation bath from the nozzle regurgitation, the inside of a gas (generally inside of air) is passed. the mileage in mind on the regurgitation side of a nozzle, and the front face of a coagulation bath (henceforth dry zone length) -- usually -- 1-50cm is especially desirable 0.1-100cm. if shorter than 0.1cm, it is choppy, and it will come out and few [a coagulation bath] things which a nozzle contacts and does to a coagulation bath for dryness-and-moisture type spinning will become difficult. Again If 100cm is exceeded, in multi-hole spinning, conglutination of the hollow fibers by yarn shake will occur. If the inside of a dry zone is made to humidify, microfacies separation and coagulation [****] will be promoted by the moisture in air, and the hollow fiber film equipped with the outside-surface layer which has the fine hole of a majority of big apertures can be obtained easily. Dry zone length this effectiveness Even if very short, it accepts as 0.1cm, and the hollow fiber film which has completely different outside-surface layer structure from the wet method directly immersed in a coagulation bath is obtained.

[0032] The configuration of the micropore of the outside-surface layer in the film can also be changed by furthermore changing the ratio (henceforth a nozzle draft) of the degree of ****** to the linear velocity in the nozzle delivery of an undiluted solution. if a nozzle draft is enlarged -- the micropore of the shape of a long and slender slit -- becoming -- easy -- reverse -- small -- rubbing -- it is easy to become comparatively circular micropore. However, since manufacture will become unstable if a nozzle draft is enlarged extremely and it is made small, a nozzle draft is usually set as the range of 2-5.

[0033] Moreover, in this invention, in order to raise the weight ratio of the vinyl-pyrrolidone system polymer which exists in the compact layer of a hollow fiber film internal surface, the internal coagulation liquid containing a vinyl-pyrrolidone system polymer is used. Although the vinyl-pyrrolidone system polymer used for internal coagulation liquid does not necessarily need to be the same as that of what was added to the undiluted solution and that from which the class differs or molecular weight differs may be used, the weight ratio which exists in an internal-surface compact layer may not improve, so that it becomes easy to be spread and the interior of the film is expected at the time of coagulation, if a polymer with small weight average molecular weight is used. Although a polymer with small weight average molecular weight can also be used by the film with precise permeable membrane etc., since the way which generally uses the thing of the with a weight average molecular weight of 100,000 or more amount of macromolecules can increase only the weight ratio which exists in an internal-surface compact layer side efficiently with a small addition, it is desirable.

[0034] The system which added the vinyl-pyrrolidone system polymer to polysulfone system polymers, such as water, alcohols, and glycols, into independent [of a non-solvent or a poor solvent] or two or more kinds of mixed liquor as internal coagulation liquid is used. Furthermore, since a coagulation rate will change and it will be useful to aperture control if a solvent is added to these, it is suitable. Especially when adding a solvent, it is desirable to make a solvent weight ratio 30 - 80% 10 to 90%. 10% or less, there is little effectiveness of a solvent, and at 90% or more, since a coagulation rate becomes very slow, spinning becomes difficult. Moreover, when the mineral salt of a lithium chloride, a zinc chloride, a sodium nitrate, etc. is added, there are desirable cases -- surface hole density increases. The vinyl-pyrrolidone system

polymer added in internal coagulation liquid is usual. 0.1 - 4 % of the weight is desirable. 0.1 or less % of the weight of the effectiveness of the increment in a weight ratio of the vinyl-pyrrolidone system polymer which exists in an internal-surface compact layer is insufficient, and it takes [washing of an excessive vinyl-pyrrolidone system polymer] time amount and is not economical if 4 % of the weight is exceeded. Moreover, there is a possibility that the weight ratio of the vinyl-pyrrolidone system polymer which exists in an internal-surface compact layer may become superfluous, and problems, such as penetrable ability and dialysis performance degradation, may occur. Therefore, it is necessary to choose about an addition, taking the class of vinyl-pyrrolidone system polymer, weight average molecular weight, the vinyl-pyrrolidone system polymer content in an undiluted solution, etc. into consideration. However, a vinyl-pyrrolidone system polymer needs to use the solution dissolved completely, and internal coagulation liquid must set it as the presentation and concentration which fulfill this condition.
[0035] If it is the independence of the non-solvent of polysulfone system polymers, such as water, alcohols, and glycols, or a poor solvent or two or more kinds of mixed liquor, and the solution that has an operation of the poor solvent of a polysulfone system polymer or a non-solvent, and has a polar solvent, polyglycols and a vinyl-pyrrolidone system polymer, and compatibility although the mixed liquor of these and a solvent is used further, there will be especially no limit in coagulation liquid.
[0036] Subsequently as for the hollow fiber film solidified by the coagulation bath, extract removal of a solvent, polyglycols, and the vinyl-pyrrolidone system polymer is carried out by rinsing or warm water washing of 40-70 degrees C or less. Under the present circumstances, although, as for polyglycols, most is extracted and, as for a vinyl-pyrrolidone system polymer, a part for a surplus is extracted, neither is extracted completely but it remains in the film. It is guessed because it is incorporated and fixed in the film in the case of coagulation as a reason polyglycols and a vinyl-pyrrolidone system polymer remain in the hollow fiber film.
[0037] Next, depending on the case, hot water processing of 80 degrees C or more is performed. stability [as opposed to / if hot water processing is performed beforehand, the washing effectiveness of a solvent, polyglycols, and a vinyl-pyrrolidone system polymer will improve upwards, and / heat] -- improving -- for example, -- Since contraction of the hollow fiber film etc. can be prevented when high-pressure-steam sterilization of 100 degrees C or more is performed, it is effective.
[0038] In this invention, the hollow fiber film is further processed after the above-mentioned process with the solution which has a poor solvent operation to a polysulfone system polymer, and extract removal of the vinyl-pyrrolidone system polymer of the whole film, especially the surplus by the side of an outside surface is performed. Although the solvent which has a poor solvent operation does not carry out the dissolution to a polysulfone system polymer, it has a certain operation of swelling etc., it says what dissolves a vinyl-pyrrolidone system polymer, and is alcohols, ethylene glycol, propylene glycol, a glycerol, and weight average molecular weight. Independent [of 600 or less polyethylene glycol], mixed liquor, or 1% of the weight or more of those water solutions can be illustrated. Moreover, although there are the approach of carrying out extract processing [after solidifying and washing the hollow fiber film] and the approach of carrying out extract processing for every module after drying the film and producing a module in an art For example, as there is no problem of conglutination not much, and the latter approach is used using the former approach when more efficient the modularization back when drying the film, and conglutination of hollow fiber film occurs and it can become a failure at the time of a modularization It can choose in consideration of manufacture conditions, process permeability,

manufacture effectiveness, cost, etc. Moreover, processing in great numbers is also possible. This processing improves manufacture stability, and since it aims at adjusting the content and distribution condition of a vinyl-pyrrolidone system polymer in the condition of having been suitable for blood processing, further, it is necessary to set up a processing liquid presentation and the processing time enough in consideration of this point.

[0039] If rinsing, heat rinsing processing, processing with the solution which has a poor solvent operation, etc. are performed, in order to carry out extract removal of excessive polyglycols and an excessive vinyl-pyrrolidone system polymer, to be incorporated in the hollow fiber film and to fix and carry out injury survival, these are hardly eluted at the time of use.

[0040] The hollow fiber film of this invention is wavelength in 10mm of layer length as an ultraviolet absorption spectrum, when the approach indicate by the eluting material test (this is call artificial kidney acknowledgement criteria for short below) of the permeable membrane of "the quality of a dialyzer and the examining method" which were showed in dialysis mold hemodialysis apparatus acknowledgement criteria estimates an effluent. 220-350nm The absorbance which can be set It is 0.1 or less and artificial kidney acknowledgement criteria are pass also in the condition as it is. Thus, the hollow fiber film of this invention structure-of-cross-linkage-izes a vinyl-pyrrolidone system polymer with the means by which heat treatment, alkali heat-treatment, gamma ray processing, etc. are conventionally well-known, and even if it does not perform specially processing which insolubilizes to water, it can use it for a blood processor, especially a dialysis mold artificial kidney.

[0041] The hollow fiber film which finished these processings is wound around a frame etc., and is dried. The dry hollow fiber film is bundled, it is fixed to housing by thermosetting polymer, such as polyurethane, and the modularization of the both ends is carried out. After sterilization processing is carried out by well-known approaches, such as EOG sterilization and autoclave sterilization, hemodialysis, hemofiltration, hemoconcentration, etc. are presented with this module as processors, such as body fluid.

[0042] By the above-mentioned manufacture approach, a vinyl-pyrrolidone system polymer is contained one to 8% of the weight at least 1% of the weight for polyglycols. The weight ratio of a polysulfone system polymer and a vinyl-pyrrolidone system polymer which exists in the internal-surface compact layer of the hollow fiber film and by 90:10-60:40 And it is even if there are few weight ratios of the vinyl-pyrrolidone system polymer to which the weight ratio of the vinyl-pyrrolidone system polymer which exists in the internal-surface compact layer of the hollow fiber film exists in an outside-surface layer. The polysulfone system hollow fiber film suitable for especially blood processing which is 1.1 times can be obtained.

[0043] The weight ratio of the polyglycols which exist in the above-mentioned hollow fiber film, and the weight ratio of a vinyl-pyrrolidone system polymer are determined by NMR, and the weight ratio of the vinyl-pyrrolidone system polymer which exists in the internal-surface compact layer and outside-surface layer of the hollow fiber film is determined by X-ray photoelectron spectroscopy (ESCA). Moreover, the module after circulate blood be disassemble as the easy evaluation approach of judge the quality of the anti-thrombus nature of the hollow fiber film, and there be the approach of measure the increment in the concentration of the fibrinopeptide A generate when the fibrinogen which be a culmination serve as a fibrin with the approach of count the number of the hollow fiber film blockade by the thrombus, the increment in the concentration of beta TOROMBO globulin which be a stripping factor by platelet damage, or the activity of a blood coagulation system.

[0044] For the following reasons, the polysulfone system hollow fiber film of this invention

needs to contain both polyglycols and a vinyl-pyrrolidone system polymer. Namely, in the internal-surface compact layer, the hollow fiber film contains a vinyl-pyrrolidone system polymer so that the weight ratio of a vinyl-pyrrolidone system polymer and a polysulfone system polymer may become 15/85. And the polysulfone system hollow fiber film which carried out spinning so that the content ratio of polyglycols might become 2 % of the weight (A), Although a vinyl-pyrrolidone system polymer is included by the weight ratio in the same internal-surface compact layer as this hollow fiber film (A) A film surface product using the hollow fiber film (B) which does not contain polyglycols, respectively After assembling the module for artificial kidneys of 2 1.7m, it applied to the same chronic-renal-failure patient's therapy. If the number of the hollow fiber which disassembled the module after use and was blockaded by blood coagulation is counted and the rate of lock out is compared Although the rate of lock out is only 5% in the artificial kidney (A) using the hollow fiber film containing polyglycols By the artificial kidney (B) using the hollow fiber film which does not contain polyglycols, the rate of lock out became 65%, and it was shown that it is very effective in the polysulfone system hollow fiber film to make a vinyl-pyrrolidone system polymer and polyglycols live together to anti-thrombus nature.

[0045] Furthermore, at least 1% of the weight of polyglycols need to exist in the polysulfone system hollow fiber film of this invention. At less than 1 % of the weight, a problem is in anti-thrombus nature and it cannot apply to blood processing.

[0046] Next, it requires that the weight ratios of a polysulfone system polymer and a vinyl-pyrrolidone system polymer which exist in the internal-surface compact layer of the polysulfone system hollow fiber film are 90:10-60:40. namely, the polysulfone system hollow fiber film which boiled, changed and manufactured various the above-mentioned ratios -- using -- effective film surface area The mini module of 500 cm2 was created and blood fresh to these was circulated. The concentration of beta TOROMBO globulin in the blood which passes a mini module, and fibrinopeptide A was contrasted with those concentration (blank) of only the blood circuits which circulate blood. About the hollow fiber film which comes to contain at least 1% of the weight of polyglycols If the weight ratio of a vinyl-pyrrolidone system polymer and a polysulfone system polymer which exists in an internal-surface compact layer is 10/90 at least The concentration of beta TOROMBO globulin and fibrinopeptide A is blank concentration, respectively. It reaches 110% or less. As opposed to being 120% or less and excelling in anti-thrombus nature The concentration of the matter which will serve as these indexes if the weight ratio of the above-mentioned vinyl-pyrrolidone system polymer and a polysulfone system polymer is less than 10/90 is blank concentration, respectively. It reaches 350%. It also becomes 400% and is inferior to anti-thrombus nature. The mini module after blood circulation was disassembled, when the number of the hollow fiber film blockaded by the thrombus was counted, and the weight ratio of a vinyl-pyrrolidone system polymer and a polysulfone system polymer was 10/90 at least, about several% of hollow fiber film blockaded and carried out, and lock out of 50% or more of hollow fiber film was observed for the above-mentioned weight ratio less than by 10/90 to that of **. On the other hand, if the weight ratio of a vinyl-pyrrolidone system polymer and a polysulfone system polymer is size from 40/60, the concentration of beta TOROMBO globulin and fibrinopeptide A is blank concentration. Although it is 105% - 110% and anti-thrombus nature is maintained, permeable ability becomes small by the swelling of a hydrophilic polymer. When the hollow fiber film contains at least 1% of the weight of polyglycols, in order to have the outstanding anti-thrombus nature from these points It is necessary to make into 10/90 at least the weight ratio of a vinyl-pyrrolidone system polymer and

polysulfone system polymer ** which exists in the compact layer of the hollow fiber film internal surface which blood contacts. In order to maintain permeable ability and the transparency engine performance of the inside molecular-weight matter, it is necessary to hold down the weight ratio of a vinyl-pyrrolidone system polymer and a polysulfone system polymer which exists in the compact layer of an internal surface to 40/60 or less.

[0047] Moreover, weight ratio of the vinyl-pyrrolidone system polymer to which the weight ratio of the vinyl-pyrrolidone system polymer which exists in a membranous internal-surface compact layer exists in an outside-surface layer in the hollow fiber film of this invention They are 1.1 or more times. thus, if a vinyl-pyrrolidone system polymer is made to exist in a hollow fiber film internal-surface compact layer so much, compared with the conventional hollow fiber film with the same weight ratio of the vinyl-pyrrolidone system polymer which exists in the inside-and-outside surface layer of the hollow fiber film, water permeability can boil more than twice and penetrable ability markedly, and the permeability of 3 or more times and an inulin can raise them. Moreover, it has the high dialysis engine performance until the hollow fiber film of this invention has the sharp (5% or less of permeability) fractionation nature which albumin hardly penetrates and results not only in low-molecular-weight matter, such as a urea, but in the beta 2-microglobulin which is low-molecular-weight protein. The reason the transparency engine performance and whose dialysis engine performance improve is because the direction made to exist in an internal-surface layer so much can make small transparency resistance by the swelling of a vinyl-pyrrolidone system polymer since it can lessen the content of the vinyl-pyrrolidone system polymer of the whole film rather than making homogeneity contain a vinyl-pyrrolidone system polymer comparatively on the whole film. in addition, weight ratio of the vinyl-pyrrolidone system polymer to which the weight ratio of the vinyl-pyrrolidone system polymer which exists in a membranous internal-surface compact layer exists in an outside-surface layer from the effect which it has on the anti-thrombus nature of the hollow fiber film 1.5 or more times -- especially -- It is desirable that they are 2.0 or more times.

[0048] Furthermore, the vinyl-pyrrolidone system polymer contained on the whole hollow fiber film usually has 2 - 5 % of the weight desirable in order to have a hydrophilic property, the outstanding permeable ability, and the transparency engine performance of the matter one to 8% of the weight. If the hydrophilic property of less than 1 % of the weight is insufficient and 8 % of the weight is exceeded, the penetrable ability and dialysis performance degradation accompanying swelling of a vinyl-pyrrolidone system polymer will happen, and physical or chemical property, such as the mechanical strength and thermal resistance which a polysulfone system polymer has further, and chemical resistance, are lost.

[0049] the hollow fiber film of this invention -- the bore -- 50-500 mum and thickness -- 5-250 mum it is . A bore is 50 micrometers. In the following, pressure loss is large and it is 500. mum If it exceeds, a module becomes large too much and handling is inconvenient. Moreover, thickness is 5 micrometers. In the following, spinning is difficult, and it is easy to generate leak, and is 250. mum If it exceeds, water permeability and dialytic will fall remarkably, and also a module becomes large and is uneconomical.

[0050] In the outside-surface layer of the hollow fiber film, it is 0.05-1 micrometer. Many fine holes exist and it is the slit width of 0.001-0.05 micrometers in an internal-surface compact layer. It has many slit-like fine holes. Moreover, cross-section structure is thickness to an internal-surface side. 0.1-3 micrometers It has the compact layer which separates the matter substantially, an aperture is gradually expanded toward a film cross-section center section, and a center section is 1-5 micrometers of average apertures. A network structure and outside-surface side is an

average aperture. 0.1-0.5 mum It is the unsymmetrical membrane structure which consisted of network structure.
[0051] By the hollow fiber film which has a compact layer a hole is not accepted to be to an outside surface Although filtration velocity is small, the penetrable ability of the low-molecular-weight protein which is the quality of a removal object, and the penetrable ability of the inside molecular weight matter of the 1000 to number of molecular weight 10,000 neighborhood also become low and the dialysis engine performance of low-molecular-weight matter, such as a urea, also falls remarkably while filtration velocity becomes slow when it uses especially for blood processing Since the polysulfone system hollow fiber film of this invention has the network structure more precise than a center section to a compact layer and an outside surface in the internal surface, it excels in a mechanical strength, and it is hard to generate leak and it can hold the outstanding solute permeability.
[0052]
[Example] Although an example explains this invention still more concretely below, thereby, this invention is not limited at all. in addition, water permeability -- the internal pressure mold lab module of 15cm of effective length -- creating -- 25 degrees C and a connoisseur -- water pressure The amount of the water which penetrated 0.5kg/cm of hollow fiber film in fixed time amount on condition that 2 was measured and computed.
[0053] moreover, each weight ratio of the polyglycols which exist in the hollow fiber film, and a vinyl-pyrrolidone system polymer -- nuclear magnetic resonance analysis (NMR) -- it measured by law. moreover, the weight ratio of the vinyl-pyrrolidone system polymer which exists in the internal-surface compact layer or outside-surface layer of the hollow fiber film -- X-ray photoelectron spectroscopy (ESCA) -- it asked as follows by law. That is, it asked for the rate of an abundance ratio of the sulfur (S) of a polysulfone system polymer, and the nitrogen (N) of a vinyl-pyrrolidone system polymer, this rate of an abundance ratio of S and N was converted into the weight (Wps) of a polysulfone system polymer, and the weight (Wvp) of a vinyl-pyrrolidone system polymer, respectively, and the weight ratio (R %) of the vinyl-pyrrolidone system polymer which exists in an internal-surface compact layer or an outside-surface layer was computed by the degree type (1).
R(%) =Wvp/(Wps+Wvp) x 100 ... (1)
[0054] Moreover, the ratio (P) of the weight ratio (Rin) of the vinyl-pyrrolidone system polymer which exists in the internal-surface compact layer of the hollow fiber film, and the weight ratio (Rout) of the vinyl-pyrrolidone system polymer which exists in an outside-surface layer was computed by the degree type (2).
P=Rin/Rout ... (2)
[0055] 17 % of the weight (it is called "PS" for short the Amoco Corp. make, YUDERU P1700, and the following) of example 1 polysulfones, Polyethylene glycol (the Sanyo Chemical Industries, Ltd. make, PEG 600, weight average molecular weight it is called "PEG" for short 600 and the following) 12.75 % of the weight, polyvinyl-pyrrolidone (product [made from GAF], K-90, weight average molecular weight it is called "PVP" for short 1,200,000 and the following) 2.55%, and dimethylacetamide (it is hereafter called "DMA" for short) 67.7% -- mixing -- heating stirring -- carrying out -- homogeneity -- the transparent undiluted solution was prepared. Outer diameter after it puts this undiluted solution for 16 hours and it carries out degassing at 45 degrees C It extruded from 0.5mm and an annular nozzle with a bore of 0.25mm in the solution which consists of 40 % of the weight of DMA, 0.5 % of the weight of PVP, and 59.5 % of the weight of water as internal coagulation liquid, and the air adjusted to discharge,

80% of relative humidity, and 50 degrees C at 50 degrees C at coincidence. It led to underwater [50-degree C], and made it solidify at the rate of 12 m/min after air transit of 10cm of dry zone length. Nozzle draft at this time It was 3.2. Subsequently, after performing immersion processing for 5 minutes into 60-degree C warm water washing and 90 degrees C hot water processing, and a 90-degree C 6-% of the weight glycerol water solution, it rolls round in a frame, and it dries, and is an outer diameter. 280 micrometers Bore 200 micrometers The hollow fiber film was obtained. Permeable ability of the obtained hollow fiber film PVP and PEG are each in 200 l/m2 and hr- (kg/cm2) and the film. The weight ratio of PVP and PS which that of exists and exists in an internal-surface compact layer 5.5% of the weight is the ratio of the weight ratio of PVP which exists in 23/77, and the weight ratio and outside-surface layer of PVP in an internal-surface compact layer. It was 2.0. [2.0] Moreover, when artificial-kidney acknowledgement criteria estimated the effluent, it is wavelength in 10mm of layer length. In a 220nm ultraviolet absorption spectrum The absorbance of 0.051 was shown and this hollow fiber film passed the above-mentioned criteria.

[0056] It is an effective film surface product in 9700 bundles about this hollow fiber film. The module for artificial kidneys of 2 was assembled 1.7m, and ethylene oxide gas sterilization, autoclave sterilization, and gamma ray sterility were respectively given to this module. Although there was almost no residual blood by hollow fiber lock out what performed ethylene oxide gas sterilization and autoclave sterilization when the module [finishing / these sterilization] was applied to the respectively same chronic-renal-failure patient and the residual blood condition (based on hollow fiber lock out) was compared, it was clearly much what gave gamma ray sterility. In addition, when the above-mentioned hollow fiber film was dissolved in chloroform, it saw, although gamma-ray-sterility processing was performed, and the insoluble solution component existed. It is thought that PVP structure-of-cross-linkage-ized this insoluble solution component, thereby, there is much residual blood and that to which anti-thrombus nature fell is presumed.

[0057] 17 % of the weight of 2PS examples, 20.4 % of the weight of PEG(s), and PVP1.7 Weight % and 60.9 % of the weight of DMA were mixed, heating stirring was carried out, and the uniform transparent undiluted solution was prepared. Outer diameter after it puts this undiluted solution for 16 hours and it carries out degassing at 45 degrees C 0.5mm, bore 0.25mm It extrudes in the air adjusted to discharge, 50 degrees C and 80% of relative humidity at 50 degrees C from the annular nozzle with the internal coagulation liquid which consists of 40 % of the weight of DMA, 0.3 % of the weight of PVP, and 59.7 % of the weight of water, and they are after air transit of 10cm of dry zone length, and 12 m/min. It led to underwater [50-degree C], and made it solidify at a rate. Nozzle draft at this time It was 3.2. Subsequently, after being immersed for 5 minutes into 60-degree C warm water washing and 90 degrees C hot water processing, and a 90-degree C 6-% of the weight GURISENRIN water solution, it winds around a frame, and it dries, and is an outer diameter. 280 micrometers Bore 200 micrometers The hollow fiber film was obtained. In addition, this hollow fiber film has no conglutination yarn after desiccation, and it was able to manufacture to stability.

[0058] This film is 10000 shown in drawing 1 . In the outside-surface layer of a twice as many scanning electron microscope photograph (it is called a SEM photograph for short below) as this to the hollow fiber film, it is 0.05-1 micrometer. It was checked that much micropores exist. Moreover, 10000 shown in drawing 2 In the internal-surface compact layer of a twice as many SEM photograph as this to the hollow fiber film, it is width of face of 0.001-0.03 micrometers. It was checked that much slit-like micropores exist. 10000 which shows the cross section by the

side of the SEM photograph in which the cross section of the 1500 times as many hollow fiber film shown in drawing 3 as this is shown, and the outside surface shown in drawing 4 A twice as many SEM photograph as this, 10000 which shows the cross section of the center section shown in drawing 5 10000 which shows the cross section by the side of the internal surface shown in twice as many a SEM photograph and drawing 6 as this From a twice as many SEM photograph as this Thickness to an internal-surface side 0.2-1 micrometer A compact layer is formed and an aperture is gradually expanded toward the center section of the film cross section. A membranous center section is 1-3 micrometers. Network structure side and outside-surface side 0.1-0.3 mum It was checked that it is the film of the unsymmetrical structure which consisted of layers which consist of precise network structure. Permeable ability of the obtained hollow fiber film PVP and PEG are each in 300 l/m2 and hr- (kg/cm2) and the film. The weight ratio of PVP and PS which those of exists and exists in an internal-surface compact layer 3.5% of the weight is the ratio of the weight ratio of PVP which exists in 23/77 and an internal-surface compact layer, and the weight ratio of PVP which exists in an outside-surface layer. It was 2.1. [2.2]
[0059] 17 % of the weight of 3PS examples, 34.0 % of the weight of PEG(s), 0.4 % of the weight of PVP, and DMA 48.6 Mixed heating stirring of the weight % was carried out, and the uniform transparent film production undiluted solution was prepared. Outer diameter after it puts this film production undiluted solution for 16 hours and it carries out degassing at 45 degrees C It extruded from 0.5mm and an annular nozzle with a bore of 0.25mm in the air adjusted to discharge, 50 degrees C, and 80% of relative humidity at 50 degrees C with the internal coagulation liquid which consists of 40 % of the weight of DMA, 1.5 % of the weight (the product made from GAF, K-120, and weight average molecular weight 250 10,000) of polyvinyl pyrrolidones, and 58.5 % of the weight of water. After air transit of 10cm of dry zone length, and 12 m/min It led to underwater [50-degree C], and made it solidify at a rate. Nozzle draft at this time It was 3.2. Subsequently, after being immersed for 5 minutes into 60-degree C warm water washing and 90 degrees C hot water processing, and a 90-degree C 5-% of the weight GURISENRIN water solution, it winds around a frame and dries, and it is an outer diameter. 280 micrometers Bore 200 micrometers The hollow fiber film was obtained. Permeable ability of the obtained hollow fiber film PVP and PEG are each in 400 l/m2 and hr- (kg/cm2) and the film. The ratio of the weight ratio of PVP to which the weight ratio of PVP and PS which that of exists and exists in an internal-surface compact layer 2.8% of the weight exists in 32/68 and an internal-surface compact layer, and the weight ratio of PVP which exists in an outside-surface layer was 16.5. [2.2] In addition, this hollow fiber film has no conglutination yarn after desiccation, and it was able to manufacture to stability.
[0060] 17 % of the weight of 4PS examples, 20.4 % of the weight of PEG(s), 1.7 % of the weight (it is called "PVP/VA" for short the product made from GAF, S630, and the following) of vinyl pyrrolidone and vinyl acetate copolymers, and 60.9 % of the weight of DMA -- mixed heating stirring -- carrying out -- homogeneity -- the transparent undiluted solution was prepared. Outer diameter after putting for 16 hours and carrying out degassing at 45 degrees C It extruded from 0.5mm and an annular nozzle with a bore of 0.25mm in the air adjusted to discharge, 50 degrees C, and 80% of relative humidity at 50 degrees C with the internal coagulation liquid which consists of 40 % of the weight of DMA, 0.5 % of the weight of PVP/VA, and 59.5 % of the weight of water. After air transit of 10cm of dry zone length, and 12 m/min It led to underwater [50-degree C], and made it solidify at a rate. Nozzle draft at this time It was 3.2. Subsequently, after being immersed for 5 minutes into 60-degree C warm water washing and 90 degrees C hot water processing, and a 30-degree C 10-% of the weight ethanol water solution, it winds around

a frame, and it dries, and is an outer diameter. 280 micrometers Bore The 200-micrometer hollow fiber film was obtained. Permeable ability of the obtained hollow fiber film 480 l/m2 and hr- (kg/cm2), PVP/VA and PEG are each in the film. 2.1 % of the weight exists 3.2% of the weight. The weight ratio of PVP/VA and PS which exists in an internal-surface compact layer is the ratio of the weight ratio of PVP/VA which exists in 21/79 and an internal-surface compact layer, and the weight ratio of PVP/VA which exists in an outside-surface layer. It was 1.7. In addition, this hollow fiber film has no conglutination yarn after desiccation, and it was able to manufacture to stability.

[0061] Mixed heating stirring of 17 % of the weight of 5PS examples, 10.2 % of the weight of PEG(s), 1.7 % of the weight of PVP, and the 71.1 % of the weight of the DMA was carried out, and the uniform transparent undiluted solution was prepared. Outer diameter after putting for 16 hours and carrying out degassing at 45 degrees C It extruded from 0.5mm and an annular nozzle with a bore of 0.25mm in the air adjusted to discharge, 50 degrees C, and 80% of relative humidity at 50 degrees C with the internal coagulation liquid which consists of 40 % of the weight of DMA, 0.5 % of the weight of PVP, and 59.5 % of the weight of water. It led to underwater [50-degree C], and made it solidify at the rate of 12 m/min after air transit of 10cm of dry zone length. Nozzle draft at this time It was 3.2. Subsequently, after being immersed for 10 minutes into 60-degree C warm water washing and 90 degrees C hot water processing, and a 80-degree C 8-% of the weight glycerol water solution, it winds around a frame, and it dries, and is an outer diameter. 280 micrometers Bore The 200-micrometer hollow fiber film was obtained. Permeable ability of the obtained hollow fiber film PVP and PEG are each in 260 l/m2 and hr- (kg/cm2) and the film. The weight ratio of PVP and PS which that of exists and exists in an internal-surface compact layer 2.8% of the weight is the ratio of the weight ratio of PVP which exists in 15/85 and an internal-surface compact layer, and the weight ratio of PVP which exists in an outside-surface layer. It was 1.9. [1.9] In addition, this hollow fiber film has no conglutination yarn after desiccation, and it was able to manufacture to stability.

[0062] Mixed heating stirring of 17 % of the weight of 1PS examples of a comparison, 34.0 % of the weight of PEG(s), and the 49.0 % of the weight of the DMA was carried out, and the uniform transparent undiluted solution was prepared. Outer diameter after putting for 16 hours and carrying out degassing at 45 degrees C It extruded from 0.5mm and an annular nozzle with a bore of 0.25mm in the air adjusted to discharge, 50 degrees C, and 80% of relative humidity at 50 degrees C with the internal coagulation liquid which consists of 40 % of the weight of DMA, and 60 % of the weight of water. After air transit of 10cm of dry zone length, and 12 m/min It led to underwater [50-degree C], and made it solidify at a rate. Nozzle draft at this time It was 3.2. Subsequently, after performing 60 degrees C warm water washing and 90-degree C hot water processing and the mesenteriolum is immersed in the 90-degree C 10 % of the weight water solution of glycerols for 15 minutes, it winds around a frame, and it dries, and is an outer diameter. 280 micrometers, bore 200 micrometers The hollow fiber film was obtained. Permeable ability of the obtained hollow fiber film It was 800 l/m2 and hr- (kg/cm2).

[0063] 17 % of the weight of 2PS examples of a comparison, water 1.0 % of the weight and PVP 6.0% of the weight, mixed heating stirring of the 76.0 % of the weight of the DMA was carried out, and the uniform transparent undiluted solution was prepared. Outer diameter after putting for 16 hours and carrying out degassing at 45 degrees C It extruded from 0.5mm and an annular nozzle with a bore of 0.25mm in the air adjusted to discharge, 50 degrees C, and 80% of relative humidity at 50 degrees C with the internal coagulation liquid which consists of 40 % of the weight of DMA, and 60 % of the weight of water. After air transit of 10cm of dry zone length,

and 12 m/min It led to underwater [50-degree C], and made it solidify at a rate. Nozzle draft at this time It was 3.2. Subsequently, after being immersed for 10 minutes into 60-degree C warm water washing and 90 degrees C hot water processing, and a 80-degree C 8-% of the weight glycerol water solution, it winds around a frame, and it dries, and is an outer diameter. 280 micrometers Bore The 200-micrometer hollow fiber film was obtained. Permeable ability of the obtained hollow fiber film The weight ratio of PVP and PS which 5 % of the weight of PVP exists in 80 l/m2 and hr- (kg/cm2) and the film, and exists in an internal-surface compact layer is the ratio of the weight ratio of PVP which exists in 16/84 and an internal-surface compact layer, and the weight ratio of PVP which exists in an outside-surface layer. It was 0.7. In addition, this hollow fiber film had very much conglutination yarn after desiccation, and it was not able to manufacture it to stability.

[0064] It extruded using the undiluted solution of example of comparison 3 example 2 in the air adjusted to discharge, 50 degrees C, and 80% of relative humidity at 50 degrees C with the internal coagulation liquid which consists of 40 % of the weight of DMA, and 60 % of the weight of water. After air transit of 10cm of dry zone length, and 12 m/min It led to underwater [50-degree C], and made it solidify at a rate. Nozzle draft at this time It was 3.2. Subsequently, after being immersed for 5 minutes into 60-degree C warm water washing and 90 degrees C hot water processing, and a 90-degree C 6-% of the weight glycerol water solution, it winds around a frame, and it dries, and is an outer diameter. 280 micrometers Bore The 200-micrometer hollow fiber film was obtained. For the permeable ability of the obtained hollow fiber film, PVP and PEG are each in 600 l/m2 and hr- (kg/cm2) and the film. Weight ratio of PVP and PS which that of exists and exists in an internal-surface compact layer 3.0% of the weight Ratio of the weight ratio of PVP which exists in 8/92 and an internal-surface compact layer, and the weight ratio of PVP which exists in an outside-surface layer It was 0.8. [2.1]

[0065] It winds around a frame, the hollow fiber film obtained by the approach of example of comparison 4 example 2 is dried, without being immersed into a glycerol water solution, after [60 degrees C] carrying out warm water washing and performing 90-degree C hot water processing, and it is an outer diameter. 280 micrometers Bore 200 micrometers Although the hollow fiber film was obtained, there was much conglutination of the hollow fiber film after desiccation, and it was not able to manufacture to stability. Moreover, permeable ability of the obtained hollow fiber film There is a problem practically very as low as 125 l/m2 and hr- (kg/cm2).

[0066] Mixed heating stirring of 17 % of the weight of 6PS examples, 22.0 % of the weight of PEG(s), 1.7 % of the weight of PVP, and the 59.3 % of the weight of the dimethylformamides was carried out, and the uniform transparent undiluted solution was prepared. Outer diameter after putting for 16 hours and carrying out degassing at 45 degrees C 0.7mm, bore From the 0.3mm annular nozzle, it extruded at 30 degrees C in discharge, 80% of relative humidity, and the air adjusted to 50 degrees C with the internal coagulation liquid which consists of 59.5 % of the weight of dimethylformamides, 0.5 % of the weight of PVP, and 40 % of the weight of water. After air transit of 10cm of dry zone length, and 10.5 m/min It led to underwater [50-degree C], and made it solidify at a rate. Nozzle draft at this time It was 3.8. Subsequently, 60 degrees C warm water washing and 90-degree C hot water processing, and 75 degrees C After being immersed for 10 minutes into a 7.5-% of the weight glycerol water solution, it winds around a frame, and it dries, and is an outer diameter. 360 micrometers Bore 230 micrometers The hollow fiber film was obtained. For the permeable ability of the obtained hollow fiber film, PVP and PEG are each in 850 l/m2 and hr- (kg/cm2) and the film. The weight ratio of PVP and PS which

that of exists and exists in an internal-surface compact layer 2.7% of the weight is the ratio of the weight ratio of PVP which exists in 20/80 and an internal-surface compact layer, and the weight ratio of PVP which exists in an outside-surface layer. It was 3.0. [1.8] In addition, this hollow fiber film has no conglutination yarn after desiccation, and it was able to manufacture to stability.

[0067] It is an effective film surface product in 9700 bundles about the hollow fiber film obtained in example 7 examples 2, 3, and 5 and the examples 1-3 of a comparison. The module for artificial kidneys of 2 was assembled 1.7m. These all performed autoclave sterilization in the wet condition. UFR (ultrafiltration rate) and the dialysis engine performance were measured based on the performance-evaluation criteria of Japanese Society for Artificial Organs using this module. Moreover, measurement of the screen multiplier of albumin and an inulin is the approach (kidney and dialysis separate volume 27 167 (1989)) shown in high performance membrane study group. It carried out. A measurement result is shown in Table 1. From Table 1, examples 2, 3, and 5 were excellent in all, such as dialysis engine performance, and, moreover, residual blood (based on lock out of a hollow fiber) was excellent in anti-thrombus nature few. On the other hand, although the example 1 of a comparison is excellent in all, such as dialysis engine performance, a problem is in anti-thrombus nature. Moreover, the examples 2 and 3 of a comparison had the low dialysis engine performance, and there was a problem also in anti-thrombus nature.

[0068]

[Table 1]

	C urea. (ml/min)	C inu. (ml/min)	S c Alb.	S c inu.	UFR 注1	残血状態 注2
実施例 2	190	103	0.001	0.99	6.4	◎
実施例 3	191	110	0.001	0.99	9.1	◎
実施例 5	185	98	0.001	0.97	5.1	○
比較例 1	195	128	0.002	0.99	17.5	×
比較例 2	158	57	0.000	0.48	2.3	△
比較例 3	192	89	0.000	0.95	12.1	×

[0069]

urea; A urea, an inu. inulin, and Alb; albumin notes 1 unit: -- ml / (min, m2, and mmHg) notes 2 residual blood: -- O; -- almost -- nothing and O; ** **; -- many [a little] x; -- ** [0070] [Effect of the Invention] As mentioned above, the polysulfone hollow fiber film of this invention Since it has the class of hydrophilic macromolecule which is especially excellent in biocompatibility, as a result anti-thrombus nature, a content, and an existence gestalt and has still higher water permeability and sharp fractionation nature If body fluid processing is performed using the polysulfone system hollow fiber film of this invention, there is no residual blood (based on lock out of a hollow fiber) by the effectiveness of the anti-thrombus nature which was excellent in hemodialysis, or since it is very few, dialysis treatment can be carried out safely, for example. Moreover, in the therapy which filters continuously like continuous hemofiltration (CAVH) for a long time, although it is little heparin administration, and there is no lock out of

the hollow fiber film by the thrombus, it is stabilized for a long time, it can use for a therapy and the inside molecular-weight matter is penetrated further, since most albumin which is useful protein is not removed, the colloidal osmotic pressure of blood is maintainable. Moreover, the viscosity control of an undiluted solution is easy for the manufacture approach of the polysulfone system hollow fiber film by this invention, and since the weight ratio of the vinyl-pyrrolidone system polymer which exists in the outside-surface layer of the hollow fiber film is low, in the production process of the hollow fiber film, it does not have conglutination of hollow fiber film and can manufacture the hollow fiber film to stability.

TECHNICAL FIELD

[Industrial Application] This invention relates to the polysulfone system hollow fiber film suitable for the blood processing which made the vinyl-pyrrolidone system polymer exist in the compact layer of the internal surface of the polysulfone system hollow fiber film and its manufacture approach, especially the hollow fiber film so much, and its manufacture approach.

PRIOR ART

[Description of the Prior Art] In recent years, the ultrafiltration method which is the separation technology using a permselectivity demarcation membrane, reverse osmosis, a gas separation method, etc. are put in practical use in various kinds of fields, and Kamiichi of the demarcation membrane made from the material which fits the various applications respectively is carried out. As a material of a permselectivity demarcation membrane, polymers, such as a cellulose system, a cellulose acetate system, a polyamide system, a polyacrylonitrile system, a polyvinyl alcohol system, a polymethylmethacrylate system, a polysulfone system, and a polyolefine system, are used. Since physicochemical qualities, such as thermal resistance, acid resistance, alkali resistance, and oxidation resistance, are excellent especially, the polysulfone system polymer attracts attention as a material of medical application and an industrial use demarcation membrane also especially recently.

[0003] However, since a polysulfone system polymer is a hydrophobic material, if the permselectivity demarcation membrane made from this is bad and water wettability dries it compared with the permselectivity demarcation membrane made from the hydrophilic polymer, the engine performance will fall. Then, the examination for giving a hydrophilic property to the permselectivity demarcation membrane which consists of a polysulfone system polymer, and raising water wettability is made, and the permselectivity demarcation membrane which made the demarcation membrane which consists of hydrophobic polymers, such as a polysulfone system polymer, contain hydrophilic polymers, such as a polyvinyl pyrrolidone, and its process are proposed as the one approach.

[0004] For example, the polysulfone system demarcation membrane which was manufactured by carrying out spinning of the undiluted solution which consists of polysulfone, with a molecular weight of 100,000 or more polyvinyl pyrrolidones, and those common solvents to JP,2-18695,B and which is made to contain a with a molecular weight of 100,000 or more polyvinyl pyrrolidone five to 70% of the weight in a demarcation membrane, and has 11% or more of water-absorption-power force, and its process are indicated. The hollow fiber film for [which is

made to contain a hydrophilic polymer one to 10% of the weight, and has 3 - 10% of water-absorption-power force] blood processing manufactured by carrying out spinning of the undiluted solution of hypoviscosity which consists of a hydrophobic polymer, hydrophilic polymers, and those common solvents to JP,61-93801,A, and its process are indicated.
[0005] JP,61-238306,A and 63-97666 -- a polysulfone system polymer, a hydrophilic polymer, and this polysulfone system polymer -- receiving -- a non-solvent -- or -- a swelling agent -- the manufacture approach of the polysulfone system demarcation membrane using the system which added the additive as a film production undiluted solution is indicated. Moreover, the method of insolubilizing a hydrophilic polymer is indicated by JP,63-97205,A and 63-97634 by performing radiation treatment and/or heat treatment to the polysulfone system demarcation membrane manufactured by the above-mentioned approach. In case spinning is furthermore carried out to JP,63-99325,A using the above-mentioned film production undiluted solution, the polysulfone system hollow fiber which smoothed the internal surface using the infusion which contains a water-soluble polymer at least 5% of the weight is indicated.
[0006] The average aperture obtained by JP,61-238834,A and 63-99325 according to the above-mentioned manufacturing method is 500. The polysulfone system porosity film whose amounts of water penetration which have the pore more than angstrom and contain a hydrophilic polymer three to 30% of the weight are more than 1000 ml/m2 and hr-mmHg is indicated. The demarcation membrane which only the compact layer side of the demarcation membrane which becomes JP,61-402,A and 62-38205 from the hydrophobic polymer which has unsymmetrical structure becomes from the mixture of this hydrophobic polymer and a hydrophilic polymer is indicated.

EFFECT OF THE INVENTION

[Effect of the Invention] As mentioned above, the polysulfone hollow fiber film of this invention Since it has the class of hydrophilic macromolecule which is especially excellent in biocompatibility, as a result anti-thrombus nature, a content, and an existence gestalt and has still higher water permeability and sharp fractionation nature If body fluid processing is performed using the polysulfone system hollow fiber film of this invention, there is no residual blood (based on lock out of a hollow fiber) by the effectiveness of the anti-thrombus nature which was excellent in hemodialysis, or since it is very few, dialysis treatment can be carried out safely, for example. Moreover, in the therapy which filters continuously like continuous hemofiltration (CAVH) for a long time, although it is little heparin administration, and there is no lock out of the hollow fiber film by the thrombus, it is stabilized for a long time, it can use for a therapy and the inside molecular-weight matter is penetrated further, since most albumin which is useful protein is not removed, the colloidal osmotic pressure of blood is maintainable. Moreover, the viscosity control of an undiluted solution is easy for the manufacture approach of the polysulfone system hollow fiber film by this invention, and since the weight ratio of the vinyl-pyrrolidone system polymer which exists in the outside-surface layer of the hollow fiber film is low, in the production process of the hollow fiber film, it does not have conglutination of hollow fiber film and can manufacture the hollow fiber film to stability.

TECHNICAL PROBLEM

[Problem(s) to be Solved by the Invention] By making a hydrophilic polymer exist in the film, the above-mentioned polysulfone system demarcation membrane gives water wettability to a hydrophobic polysulfone system demarcation membrane, and raises permeable ability, and moreover, although it has the outstanding engine performance -- contamination of the film by protein adsorption etc. is prevented -- sufficient examination about biocompatibility is not made and it is not necessarily satisfied in respect of anti-thrombus nature.

[0008] For example, the polysulfone system hollow fiber film suitable for blood processing is indicated by JP,61-93801,A. although a detail in the letter has the publication of the purport which is the film which can suppress complement activity low about this hollow fiber film, the property that complement activity is suppressed low is a property discovered only when the hollow fiber film is hydrophobicity. That is, hydrophilization of the internal surface which blood contacts was not fully carried out, but the hollow fiber film indicated by JP,61-93801,A has suggested that hydrophobicity still remains. When hydrophobicity remains in the front face on which blood contacts, it is in the condition that a platelet tends to adhere. Once a platelet adheres to the internal surface of the hollow fiber film, the matter which activates a blood coagulation system by condensation of a platelet and collapse will be emitted, and blood coagulation will arise.

[0009] Moreover, since the polysulfone system demarcation membrane indicated by JP,2-18695,B has 11% or more of water absorption power, it absorbs the moisture in air during the preservation after film production. Therefore, a facility special for demarcation membrane preservation is needed. Moreover, since that water absorption power is high has much abundance of the polyvinyl pyrrolidone in a demarcation membrane, the mechanical engine performance of a demarcation membrane falls and permeable ability also falls.

[0010] Since the polysulfone system demarcation membrane indicated by a process or JP,61-238834,A of a polysulfone system demarcation membrane furthermore indicated by JP,61-238306,A, JP,63-99325,A, etc. has added the hydrophilic polymer to the film production undiluted solution, it cannot fully carry out hydrophilization of the internal surface of a demarcation membrane like the polysulfone system hollow fiber film indicated by JP,61-93801,A. Moreover, this process Although it is suitable for the process of the demarcation membrane which has a big hole 500A or more, it is not suitable for the process of the demarcation membrane for hemodialysis. Although the process of the polysulfone system demarcation membrane indicated by JP,63-99325,A is making the water-soluble polymer contain in internal coagulation liquid, a water-soluble polymer is not made to remain in the internal surface of the hollow fiber film only by this polymer having given smooth nature to the internal surface of a hollow fiber.

[0011] Since hydrophilization only of the compact layer is only carried out, if the polysulfone system demarcation membrane which has the unsymmetrical structure indicated by JP,61-402,A and 62-38205 dries a demarcation membrane, water permeability will fall remarkably. Moreover, protein adsorption in the part by which hydrophilization is not carried out arises.

[0012] Therefore, the purpose of this invention is excellent in the biocompatibility which solved the above-mentioned problem of the conventional polysulfone system demarcation membrane, and it is in offering the polysulfone system hollow fiber film suitable for especially blood processing without a permeable fall, after drying. Other purposes of this invention are to offer

the manufacture approach of the above-mentioned polysulfone system hollow fiber film.

MEANS

[Means for Solving the Problem] The place which examined a conventional polysulfone system hollow fiber and its conventional manufacture approach that this invention persons should attain the above-mentioned technical problem, If a hollow fiber is made to contain polyglycols and a vinyl-pyrrolidone system polymer also unexpectedly and a vinyl-pyrrolidone system polymer is made to exist in the internal surface of a hollow fiber so much This invention is reached [that the hollow fiber film having the physicochemical engine performance which was excellent in the polysulfone system polymer, and the engine performance of both hydrophilic properties which was excellent in the vinyl-pyrrolidone system polymer excellent in especially anti-thrombus nature can be offered, and] as a result of inquiring further, a header and.

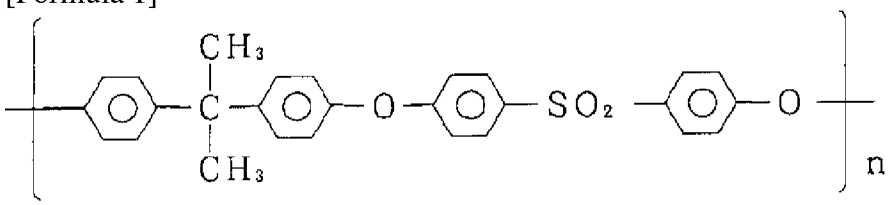
[0014] Namely, the polysulfone system hollow fiber film of this invention It is the hollow fiber film of the unsymmetrical structure which has a compact layer in an internal surface which consists of a polysulfone system polymer. This hollow fiber film uses a polysulfone system polymer as a principal component, and contains at least 1% of the weight of polyglycols, and 1 - 8% of the weight of a vinyl-pyrrolidone system polymer. The weight ratio of a polysulfone system polymer and a vinyl-pyrrolidone system polymer which exists in the compact layer of the internal surface of the hollow fiber film and by 90:10-60:40 And it is even if there are few weight ratios of the vinyl-pyrrolidone system polymer to which the weight ratio of the vinyl-pyrrolidone system polymer which exists in the above-mentioned compact layer of the internal surface of the hollow fiber film exists in an outside-surface layer. It is characterized by being 1.1 times.

[0015] Moreover, the manufacture approach of the polysulfone system hollow fiber film concerning this invention A polysulfone system polymer and weight average molecular weight The process which makes the film production undiluted solution with which the polyglycols and weight average molecular weight of 200-6000 carried out the mixed dissolution of the vinyl-pyrrolidone system polymer of at least 10000 breathe out from an annular orifice, The process which supplies the solution containing 0.1 - 4% of the weight of a vinyl-pyrrolidone system polymer to the interior of the annular flow of the above-mentioned regurgitation undiluted solution, and forms the polysulfone system hollow fiber film, The produced this polysulfone system hollow fiber film is processed with the solution which has a poor solvent operation to this polysulfone system polymer. Even if there are few weight ratios of the vinyl-pyrrolidone system polymer to which the weight ratio of the vinyl-pyrrolidone system polymer which exists in the compact layer of the internal surface of the hollow fiber film exists in an outside-surface layer It is characterized by coming to contain the process adjusted so that it may become 1.1 times.

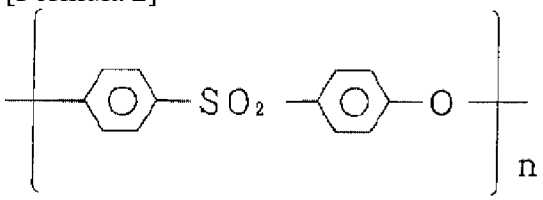
[0016] Fundamentally, a polysulfone system polymer and weight average molecular weight the undiluted solution used in order to manufacture the polysulfone system hollow fiber film of this invention It consists of 4 component systems which the polyglycols of 200-6000 and weight average molecular weight become from the common solvent of the vinyl-pyrrolidone system polymer of at least 10,000, and these polymers.

[0017] Although a polysulfone system polymer consists of a repeat unit usually shown with a chemical formula (1) or a chemical formula (2), it may also contain functional groups, such as an alkyl system and a sulfone radical.

[0018]
[Formula 1]



[0019]
[Formula 2]



[0020] The concentration of the polysulfone system polymer contained in an undiluted solution is usually 15 - 20 % of the weight preferably ten to 25% of the weight that what is necessary is just the density range which enables manufacture of the hollow fiber film which has the property which suited the purpose application. It becomes impossible to obtain sufficient reinforcement as hollow fiber film, and to form the practical hollow fiber film at less than 10 % of the weight. Moreover, it is not practical in order for a through tube to decrease and to cause membranous penetrable ability and dialysis performance degradation, if 25 % of the weight is exceeded.
[0021] Weight average molecular weight polyglycols with a polyethylene glycol, polypropylene glycols, these copolymers or these ester, an amine, the ether, and an acetal derivative The polymer of 200-6000 is used. In this invention, in order to add polyglycols in an undiluted solution, there are the following advantages. since an operation of the 1st of polyglycols has an operation of a poor solvent to polysulfone first -- a fine hole -- if it is effective as a formation agent and this is added, the microfacies separation effectiveness will improve and the porous film with high void content and surface hole density will form -- having -- being easy -- the demarcation membrane which has the outstanding penetrable ability and the outstanding dialysis engine performance can be obtained.
[0022] the 2nd -- a fine hole -- there is the thickening effectiveness of an undiluted solution compared with the water usually used as a formation agent, alcohols, a glycerol, mineral, etc., and since there is moreover no abrupt change of the viscosity by the addition, in order to manufacture the hollow fiber film, the undiluted solution which has suitable viscosity can be prepared easily.
[0023] If polyglycols are added in an undiluted solution to the 3rd, the inclination for the content effectiveness of the vinyl-pyrrolidone system polymer made to remain in the film to improve is accepted so that it may mention later, and the hollow fiber film can be made to contain a vinyl-pyrrolidone system polymer efficiently also with a small addition. although the reason whose content effectiveness of a vinyl-pyrrolidone system polymer improves is unknown if polyglycols are added in an undiluted solution -- the fine hole of others [polyglycols] -- the behavior of coagulation differs as compared with a formation agent, or the reasons of playing the role like a dispersant can be considered. Since a vinyl-pyrrolidone system polymer can make this vinyl-pyrrolidone system polymer contain in the hollow fiber film efficiently also with a small addition

even if it carries out in any, it is advantageous in respect of content ratio adjustment of a cost side or a vinyl-pyrrolidone system polymer. Moreover, since the addition of a vinyl-pyrrolidone system polymer can be lessened, it is easy to hold down undiluted solution viscosity to the range where spinning is stable.

[0024] Although the polyglycols added in the undiluted solution to the 4th are not removed completely but an amount remains in the film a little, the inclination for anti-thrombus nature to be reinforced by making polyglycols and a vinyl-pyrrolidone system polymer live together in the film is accepted.

[0025] Thus, there are many advantageous points by using polyglycols. Although the addition of the polyglycols to the inside of an undiluted solution changes in this invention with classes of the weight average molecular weight of polyglycols, polysulfone system polymer concentration, or solvent in order to demonstrate above-mentioned effectiveness effectively, it is 50-300 to a polysulfone system polymer. Weight %, usual 100-200 It is desirable to do weight % addition of.

[0026] A vinyl-pyrrolidone system polymer remains mainly on the polysulfone system hollow fiber film, a hydrophilic property is made to give the hydrophobic polysulfone system hollow fiber film, and the polymer of at least 10,000 is used for a polymer with larger weight average molecular weight than polyglycols, and usual weight average molecular weight. As this vinyl-pyrrolidone system polymer, a polyvinyl pyrrolidone, vinyl pyrrolidone and a vinyl acetate copolymer, a vinyl-pyrrolidone vinyl alcohol copolymer, a vinyl-pyrrolidone styrene copolymer, vinyl-pyrrolidone dimethylaminoethyl methacrylate copolymers, etc. and these denaturation polymers are mentioned.

[0027] Although it is necessary to make the amount which demonstrates hydrophilic effectiveness remain in the film, if a vinyl-pyrrolidone system polymer is added in large quantities in an undiluted solution, the viscosity of an undiluted solution increases rapidly, manufacture of the hollow fiber film will become difficult, and a vinyl-pyrrolidone system polymer will require time amount for the extract of an excessive vinyl-pyrrolidone system polymer, and it will be easy to become inadequate washing it. If the hollow fiber film is furthermore dried, the migration by the side of the outside surface of the hollow fiber film of a vinyl-pyrrolidone system polymer becomes remarkable, and conglutination of hollow fibers will occur and it will become a failure at the time of handling and modularization of the hollow fiber film. If the addition of a vinyl-pyrrolidone system polymer furthermore increases, the content weight ratio in the hollow fiber film will increase, and physical and the water permeability ability accompanying [while chemical property is spoiled] the swelling of a vinyl-pyrrolidone system polymer, or dialysis performance degradation, such as the mechanical strength and thermal resistance which a polysulfone system polymer has, and chemical resistance, will be caused.

[0028] Therefore, it is not necessarily desirable to add a vinyl-pyrrolidone system polymer in large quantities in an undiluted solution. The minimum amount of the addition of the vinyl-pyrrolidone system polymer to the inside of an undiluted solution which gives a hydrophilic property to the polysulfone system hollow fiber film is desirable. The addition of a vinyl-pyrrolidone system polymer is usually added five to 15% of the weight two to 30% of the weight to a polysulfone system polymer.

[0029] A solvent dissolves all of a polysulfone system polymer, polyglycols, and a vinyl-pyrrolidone system polymer, and although the solvent of varieties, such as dimethylformamide, dimethylacetamide, a N-methyl-2-pyrrolidone, dimethyl sulfoxide, a sulfolane, and dioxane, or the solvent which consists of the two or more above-mentioned kinds of mixed liquor is used, especially dimethylformamide and dimethylacetamide are used preferably.

[0030] An undiluted solution with various descriptions can be obtained with the combination of the above-mentioned presentation. For example, if the addition of polyglycols is made [many], using a soluble low solvent, the undiluted solution which carries out phase separation of beyond specific temperature or below specific temperature will be obtained. If spinning is carried out near phase separation temperature using this undiluted solution, the hollow fiber film which has a comparatively porous hole suitable for precision filtration etc. can be manufactured. On the contrary, using a soluble good solvent, if the addition of polyglycols is lessened, the precise film which became the shape of comparatively stable Hara acidity or alkalinity, and fitted an ultrafiltration, dialysis, etc. can be manufactured.
[0031] The polysulfone system hollow fiber film is obtained using the undiluted solution which consists of the above system. Film production actuation can use a well-known dryness-and-moisture type method, and the above-mentioned undiluted solution and internal coagulation liquid which were kept warm by fixed temperature are breathed out by coincidence from the annular nozzle of double tubing structure, and it is introduced into a coagulation bath. By the dryness-and-moisture type method, before being immersed in a coagulation bath from the nozzle regurgitation, the inside of a gas (generally inside of air) is passed. the mileage in mind on the regurgitation side of a nozzle, and the front face of a coagulation bath (henceforth dry zone length) -- usually -- 1-50cm is especially desirable 0.1-100cm. if shorter than 0.1cm, it is choppy, and it will come out and few [a coagulation bath] things which a nozzle contacts and does to a coagulation bath for dryness-and-moisture type spinning will become difficult. Again If 100cm is exceeded, in multi-hole spinning, conglutination of the hollow fibers by yarn shake will occur. If the inside of a dry zone is made to humidify, microfacies separation and coagulation [****] will be promoted by the moisture in air, and the hollow fiber film equipped with the outside-surface layer which has the fine hole of a majority of big apertures can be obtained easily. Dry zone length this effectiveness Even if very short, it accepts as 0.1cm, and the hollow fiber film which has completely different outside-surface layer structure from the wet method directly immersed in a coagulation bath is obtained.
[0032] The configuration of the micropore of the outside-surface layer in the film can also be changed by furthermore changing the ratio (henceforth a nozzle draft) of the degree of ****** to the linear velocity in the nozzle delivery of an undiluted solution. if a nozzle draft is enlarged -- the micropore of the shape of a long and slender slit -- becoming -- easy -- reverse -- small -- rubbing -- it is easy to become comparatively circular micropore. However, since manufacture will become unstable if a nozzle draft is enlarged extremely and it is made small, a nozzle draft is usually set as the range of 2-5.
[0033] Moreover, in this invention, in order to raise the weight ratio of the vinyl-pyrrolidone system polymer which exists in the compact layer of a hollow fiber film internal surface, the internal coagulation liquid containing a vinyl-pyrrolidone system polymer is used. Although the vinyl-pyrrolidone system polymer used for internal coagulation liquid does not necessarily need to be the same as that of what was added to the undiluted solution and that from which the class differs or molecular weight differs may be used, the weight ratio which exists in an internal-surface compact layer may not improve, so that it becomes easy to be spread and the interior of the film is expected at the time of coagulation, if a polymer with small weight average molecular weight is used. Although a polymer with small weight average molecular weight can also be used by the film with precise permeable membrane etc., since the way which generally uses the thing of the with a weight average molecular weight of 100,000 or more amount of macromolecules can increase only the weight ratio which exists in an internal-surface compact

layer side efficiently with a small addition, it is desirable.
[0034] The system which added the vinyl-pyrrolidone system polymer to polysulfone system polymers, such as water, alcohols, and glycols, into independent [of a non-solvent or a poor solvent] or two or more kinds of mixed liquor as internal coagulation liquid is used. Furthermore, since a coagulation rate will change and it will be useful to aperture control if a solvent is added to these, it is suitable. Especially when adding a solvent, it is desirable to make a solvent weight ratio 30 - 80% 10 to 90%. 10% or less, there is little effectiveness of a solvent, and at 90% or more, since a coagulation rate becomes very slow, spinning becomes difficult. Moreover, when the mineral salt of a lithium chloride, a zinc chloride, a sodium nitrate, etc. is added, there are desirable cases -- surface hole density increases. The vinyl-pyrrolidone system polymer added in internal coagulation liquid is usual. 0.1 - 4 % of the weight is desirable. 0.1 or less % of the weight of the effectiveness of the increment in a weight ratio of the vinyl-pyrrolidone system polymer which exists in an internal-surface compact layer is insufficient, and it takes [washing of an excessive vinyl-pyrrolidone system polymer] time amount and is not economical if 4 % of the weight is exceeded. Moreover, there is a possibility that the weight ratio of the vinyl-pyrrolidone system polymer which exists in an internal-surface compact layer may become superfluous, and problems, such as penetrable ability and dialysis performance degradation, may occur. Therefore, it is necessary to choose about an addition, taking the class of vinyl-pyrrolidone system polymer, weight average molecular weight, the vinyl-pyrrolidone system polymer content in an undiluted solution, etc. into consideration. However, a vinyl-pyrrolidone system polymer needs to use the solution dissolved completely, and internal coagulation liquid must set it as the presentation and concentration which fulfill this condition.
[0035] If it is the independence of the non-solvent of polysulfone system polymers, such as water, alcohols, and glycols, or a poor solvent or two or more kinds of mixed liquor, and the solution that has an operation of the poor solvent of a polysulfone system polymer or a non-solvent, and has a polar solvent, polyglycols and a vinyl-pyrrolidone system polymer, and compatibility although the mixed liquor of these and a solvent is used further, there will be especially no limit in coagulation liquid.
[0036] Subsequently as for the hollow fiber film solidified by the coagulation bath, extract removal of a solvent, polyglycols, and the vinyl-pyrrolidone system polymer is carried out by rinsing or warm water washing of 40-70 degrees C or less. Under the present circumstances, although, as for polyglycols, most is extracted and, as for a vinyl-pyrrolidone system polymer, a part for a surplus is extracted, neither is extracted completely but it remains in the film. It is guessed because it is incorporated and fixed in the film in the case of coagulation as a reason polyglycols and a vinyl-pyrrolidone system polymer remain in the hollow fiber film.
[0037] Next, depending on the case, hot water processing of 80 degrees C or more is performed. stability [as opposed to / if hot water processing is performed beforehand, the washing effectiveness of a solvent, polyglycols, and a vinyl-pyrrolidone system polymer will improve upwards, and / heat] -- improving -- for example, -- Since contraction of the hollow fiber film etc. can be prevented when high-pressure-steam sterilization of 100 degrees C or more is performed, it is effective.
[0038] In this invention, the hollow fiber film is further processed after the above-mentioned process with the solution which has a poor solvent operation to a polysulfone system polymer, and extract removal of the vinyl-pyrrolidone system polymer of the whole film, especially the surplus by the side of an outside surface is performed. Although the solvent which has a poor solvent operation does not carry out the dissolution to a polysulfone system polymer, it has a

certain operation of swelling etc., it says what dissolves a vinyl-pyrrolidone system polymer, and is alcohols, ethylene glycol, propylene glycol, a glycerol, and weight average molecular weight. Independent [of 600 or less polyethylene glycol], mixed liquor, or 1% of the weight or more of those water solutions can be illustrated. Moreover, although there are the approach of carrying out extract processing [after solidifying and washing the hollow fiber film] and the approach of carrying out extract processing for every module after drying the film and producing a module in an art For example, as there is no problem of conglutination not much, and the latter approach is used using the former approach when more efficient the modularization back when drying the film, and conglutination of hollow fiber film occurs and it can become a failure at the time of a modularization It can choose in consideration of manufacture conditions, process permeability, manufacture effectiveness, cost, etc. Moreover, processing in great numbers is also possible. This processing improves manufacture stability, and since it aims at adjusting the content and distribution condition of a vinyl-pyrrolidone system polymer in the condition of having been suitable for blood processing, further, it is necessary to set up a processing liquid presentation and the processing time enough in consideration of this point.

[0039] If rinsing, heat rinsing processing, processing with the solution which has a poor solvent operation, etc. are performed, in order to carry out extract removal of excessive polyglycols and an excessive vinyl-pyrrolidone system polymer, to be incorporated in the hollow fiber film and to fix and carry out injury survival, these are hardly eluted at the time of use.

[0040] The hollow fiber film of this invention is wavelength in 10mm of layer length as an ultraviolet absorption spectrum, when the approach indicate by the eluting material test (this is call artificial kidney acknowledgement criteria for short below) of the permeable membrane of "the quality of a dialyzer and the examining method" which were showed in dialysis mold hemodialysis apparatus acknowledgement criteria estimates an effluent. 220-350nm The absorbance which can be set It is 0.1 or less and artificial kidney acknowledgement criteria are pass also in the condition as it is. Thus, the hollow fiber film of this invention structure-of-cross-linkage-izes a vinyl-pyrrolidone system polymer with the means by which heat treatment, alkali heat-treatment, gamma ray processing, etc. are conventionally well-known, and even if it does not perform specially processing which insolubilizes to water, it can use it for a blood processor, especially a dialysis mold artificial kidney.

[0041] The hollow fiber film which finished these processings is wound around a frame etc., and is dried. The dry hollow fiber film is bundled, it is fixed to housing by thermosetting polymer, such as polyurethane, and the modularization of the both ends is carried out. After sterilization processing is carried out by well-known approaches, such as EOG sterilization and autoclave sterilization, hemodialysis, hemofiltration, hemoconcentration, etc. are presented with this module as processors, such as body fluid.

[0042] By the above-mentioned manufacture approach, a vinyl-pyrrolidone system polymer is contained one to 8% of the weight at least 1% of the weight for polyglycols. The weight ratio of a polysulfone system polymer and a vinyl-pyrrolidone system polymer which exists in the internal-surface compact layer of the hollow fiber film and by 90:10-60:40 And it is even if there are few weight ratios of the vinyl-pyrrolidone system polymer to which the weight ratio of the vinyl-pyrrolidone system polymer which exists in the internal-surface compact layer of the hollow fiber film exists in an outside-surface layer. The polysulfone system hollow fiber film suitable for especially blood processing which is 1.1 times can be obtained.

[0043] The weight ratio of the polyglycols which exist in the above-mentioned hollow fiber film, and the weight ratio of a vinyl-pyrrolidone system polymer are determined by NMR, and the

weight ratio of the vinyl-pyrrolidone system polymer which exists in the internal-surface compact layer and outside-surface layer of the hollow fiber film is determined by X-ray photoelectron spectroscopy (ESCA). Moreover, the module after circulate blood be disassemble as the easy evaluation approach of judge the quality of the anti-thrombus nature of the hollow fiber film, and there be the approach of measure the increment in the concentration of the fibrinopeptide A generate when the fibrinogen which be a culmination serve as a fibrin with the approach of count the number of the hollow fiber film blockade by the thrombus, the increment in the concentration of beta TOROMBO globulin which be a stripping factor by platelet damage, or the activity of a blood coagulation system.

[0044] For the following reasons, the polysulfone system hollow fiber film of this invention needs to contain both polyglycols and a vinyl-pyrrolidone system polymer. Namely, in the internal-surface compact layer, the hollow fiber film contains a vinyl-pyrrolidone system polymer so that the weight ratio of a vinyl-pyrrolidone system polymer and a polysulfone system polymer may become 15/85. And the polysulfone system hollow fiber film which carried out spinning so that the content ratio of polyglycols might become 2 % of the weight (A), Although a vinyl-pyrrolidone system polymer is included by the weight ratio in the same internal-surface compact layer as this hollow fiber film (A) A film surface product using the hollow fiber film (B) which does not contain polyglycols, respectively After assembling the module for artificial kidneys of 2 1.7m, it applied to the same chronic-renal-failure patient's therapy. If the number of the hollow fiber which disassembled the module after use and was blockaded by blood coagulation is counted and the rate of lock out is compared Although the rate of lock out is only 5% in the artificial kidney (A) using the hollow fiber film containing polyglycols By the artificial kidney (B) using the hollow fiber film which does not contain polyglycols, the rate of lock out became 65%, and it was shown that it is very effective in the polysulfone system hollow fiber film to make a vinyl-pyrrolidone system polymer and polyglycols live together to anti-thrombus nature.

[0045] Furthermore, at least 1% of the weight of polyglycols need to exist in the polysulfone system hollow fiber film of this invention. At less than 1 % of the weight, a problem is in anti-thrombus nature and it cannot apply to blood processing.

[0046] Next, it requires that the weight ratios of a polysulfone system polymer and a vinyl-pyrrolidone system polymer which exist in the internal-surface compact layer of the polysulfone system hollow fiber film are 90:10-60:40. namely, the polysulfone system hollow fiber film which boiled, changed and manufactured various the above-mentioned ratios -- using -- effective film surface area The mini module of 500 cm2 was created and blood fresh to these was circulated. The concentration of beta TOROMBO globulin in the blood which passes a mini module, and fibrinopeptide A was contrasted with those concentration (blank) of only the blood circuits which circulate blood. About the hollow fiber film which comes to contain at least 1% of the weight of polyglycols If the weight ratio of a vinyl-pyrrolidone system polymer and a polysulfone system polymer which exists in an internal-surface compact layer is 10/90 at least The concentration of beta TOROMBO globulin and fibrinopeptide A is blank concentration, respectively. It reaches 110% or less. As opposed to being 120% or less and excelling in anti-thrombus nature The concentration of the matter which will serve as these indexes if the weight ratio of the above-mentioned vinyl-pyrrolidone system polymer and a polysulfone system polymer is less than 10/90 is blank concentration, respectively. It reaches 350%. It also becomes 400% and is inferior to anti-thrombus nature. The mini module after blood circulation was disassembled, when the number of the hollow fiber film blockaded by the thrombus was counted,

and the weight ratio of a vinyl-pyrrolidone system polymer and a polysulfone system polymer was 10/90 at least, about several% of hollow fiber film blockaded and carried out, and lock out of 50% or more of hollow fiber film was observed for the above-mentioned weight ratio less than by 10/90 to that of **. On the other hand, if the weight ratio of a vinyl-pyrrolidone system polymer and a polysulfone system polymer is size from 40/60, the concentration of beta TOROMBO globulin and fibrinopeptide A is blank concentration. Although it is 105% - 110% and anti-thrombus nature is maintained, permeable ability becomes small by the swelling of a hydrophilic polymer. When the hollow fiber film contains at least 1% of the weight of polyglycols, in order to have the outstanding anti-thrombus nature from these points It is necessary to make into 10/90 at least the weight ratio of a vinyl-pyrrolidone system polymer and polysulfone system polymer ** which exists in the compact layer of the hollow fiber film internal surface which blood contacts. In order to maintain permeable ability and the transparency engine performance of the inside molecular-weight matter, it is necessary to hold down the weight ratio of a vinyl-pyrrolidone system polymer and a polysulfone system polymer which exists in the compact layer of an internal surface to 40/60 or less.

[0047] Moreover, weight ratio of the vinyl-pyrrolidone system polymer to which the weight ratio of the vinyl-pyrrolidone system polymer which exists in a membranous internal-surface compact layer exists in an outside-surface layer in the hollow fiber film of this invention They are 1.1 or more times. thus, if a vinyl-pyrrolidone system polymer is made to exist in a hollow fiber film internal-surface compact layer so much, compared with the conventional hollow fiber film with the same weight ratio of the vinyl-pyrrolidone system polymer which exists in the inside-and-outside surface layer of the hollow fiber film, water permeability can boil more than twice and penetrable ability markedly, and the permeability of 3 or more times and an inulin can raise them. Moreover, it has the high dialysis engine performance until the hollow fiber film of this invention has the sharp (5% or less of permeability) fractionation nature which albumin hardly penetrates and results not only in low-molecular-weight matter, such as a urea, but in the beta 2-microglobulin which is low-molecular-weight protein. The reason the transparency engine performance and whose dialysis engine performance improve is because the direction made to exist in an internal-surface layer so much can make small transparency resistance by the swelling of a vinyl-pyrrolidone system polymer since it can lessen the content of the vinyl-pyrrolidone system polymer of the whole film rather than making homogeneity contain a vinyl-pyrrolidone system polymer comparatively on the whole film. in addition, weight ratio of the vinyl-pyrrolidone system polymer to which the weight ratio of the vinyl-pyrrolidone system polymer which exists in a membranous internal-surface compact layer exists in an outside-surface layer from the effect which it has on the anti-thrombus nature of the hollow fiber film 1.5 or more times -- especially -- It is desirable that they are 2.0 or more times.

[0048] Furthermore, the vinyl-pyrrolidone system polymer contained on the whole hollow fiber film usually has 2 - 5 % of the weight desirable in order to have a hydrophilic property, the outstanding permeable ability, and the transparency engine performance of the matter one to 8% of the weight. If the hydrophilic property of less than 1 % of the weight is insufficient and 8 % of the weight is exceeded, the penetrable ability and dialysis performance degradation accompanying swelling of a vinyl-pyrrolidone system polymer will happen, and physical or chemical property, such as the mechanical strength and thermal resistance which a polysulfone system polymer has further, and chemical resistance, are lost.

[0049] the hollow fiber film of this invention -- the bore -- 50-500 mum and thickness -- 5-250 mum it is . A bore is 50 micrometers. In the following, pressure loss is large and it is 500. mum

If it exceeds, a module becomes large too much and handling is inconvenient. Moreover, thickness is 5 micrometers. In the following, spinning is difficult, and it is easy to generate leak, and is 250. mum If it exceeds, water permeability and dialytic will fall remarkably, and also a module becomes large and is uneconomical.

[0050] In the outside-surface layer of the hollow fiber film, it is 0.05-1 micrometer. Many fine holes exist and it is the slit width of 0.001-0.05 micrometers in an internal-surface compact layer. It has many slit-like fine holes. Moreover, cross-section structure is thickness to an internal-surface side. 0.1-3 micrometers It has the compact layer which separates the matter substantially, an aperture is gradually expanded toward a film cross-section center section, and a center section is 1-5 micrometers of average apertures. A network structure and outside-surface side is an average aperture. 0.1-0.5 mum It is the unsymmetrical membrane structure which consisted of network structure.

[0051] By the hollow fiber film which has a compact layer a hole is not accepted to be to an outside surface Although filtration velocity is small, the penetrable ability of the low-molecular-weight protein which is the quality of a removal object, and the penetrable ability of the inside molecular weight matter of the 1000 to number of molecular weight 10,000 neighborhood also become low and the dialysis engine performance of low-molecular-weight matter, such as a urea, also falls remarkably while filtration velocity becomes slow when it uses especially for blood processing Since the polysulfone system hollow fiber film of this invention has the network structure more precise than a center section to a compact layer and an outside surface in the internal surface, it excels in a mechanical strength, and it is hard to generate leak and it can hold the outstanding solute permeability.

EXAMPLE

[Example] Although an example explains this invention still more concretely below, thereby, this invention is not limited at all. in addition, water permeability -- the internal pressure mold lab module of 15cm of effective length -- creating -- 25 degrees C and a connoisseur -- water pressure The amount of the water which penetrated 0.5kg/cm of hollow fiber film in fixed time amount on condition that 2 was measured and computed.

[0053] moreover, each weight ratio of the polyglycols which exist in the hollow fiber film, and a vinyl-pyrrolidone system polymer -- nuclear magnetic resonance analysis (NMR) -- it measured by law. moreover, the weight ratio of the vinyl-pyrrolidone system polymer which exists in the internal-surface compact layer or outside-surface layer of the hollow fiber film -- X-ray photoelectron spectroscopy (ESCA) -- it asked as follows by law. That is, it asked for the rate of an abundance ratio of the sulfur (S) of a polysulfone system polymer, and the nitrogen (N) of a vinyl-pyrrolidone system polymer, this rate of an abundance ratio of S and N was converted into the weight (Wps) of a polysulfone system polymer, and the weight (Wvp) of a vinyl-pyrrolidone system polymer, respectively, and the weight ratio (R %) of the vinyl-pyrrolidone system polymer which exists in an internal-surface compact layer or an outside-surface layer was computed by the degree type (1).

$$R(\%) = Wvp/(Wps+Wvp) \times 100 \quad \ldots (1)$$

[0054] Moreover, the ratio (P) of the weight ratio (Rin) of the vinyl-pyrrolidone system polymer which exists in the internal-surface compact layer of the hollow fiber film, and the weight ratio (Rout) of the vinyl-pyrrolidone system polymer which exists in an outside-surface layer was

computed by the degree type (2).
P=Rin/Rout ... (2)
[0055] 17 % of the weight (it is called "PS" for short the Amoco Corp. make, YUDERU P1700, and the following) of example 1 polysulfones, Polyethylene glycol (the Sanyo Chemical Industries, Ltd. make, PEG 600, weight average molecular weight it is called "PEG" for short 600 and the following) 12.75 % of the weight, polyvinyl-pyrrolidone (product [made from GAF], K-90, weight average molecular weight it is called "PVP" for short 1,200,000 and the following) 2.55%, and dimethylacetamide (it is hereafter called "DMA" for short) 67.7% -- mixing -- heating stirring -- carrying out -- homogeneity -- the transparent undiluted solution was prepared. Outer diameter after it puts this undiluted solution for 16 hours and it carries out degassing at 45 degrees C It extruded from 0.5mm and an annular nozzle with a bore of 0.25mm in the solution which consists of 40 % of the weight of DMA, 0.5 % of the weight of PVP, and 59.5 % of the weight of water as internal coagulation liquid, and the air adjusted to discharge, 80% of relative humidity, and 50 degrees C at 50 degrees C at coincidence. It led to underwater [50-degree C], and made it solidify at the rate of 12 m/min after air transit of 10cm of dry zone length. Nozzle draft at this time It was 3.2. Subsequently, after performing immersion processing for 5 minutes into 60-degree C warm water washing and 90 degrees C hot water processing, and a 90-degree C 6-% of the weight glycerol water solution, it rolls round in a frame, and it dries, and is an outer diameter. 280 micrometers Bore 200 micrometers The hollow fiber film was obtained. Permeable ability of the obtained hollow fiber film PVP and PEG are each in 200 l/m2 and hr- (kg/cm2) and the film. The weight ratio of PVP and PS which that of exists and exists in an internal-surface compact layer 5.5% of the weight is the ratio of the weight ratio of PVP which exists in 23/77, and the weight ratio and outside-surface layer of PVP in an internal-surface compact layer. It was 2.0. [2.0] Moreover, when artificial-kidney acknowledgement criteria estimated the effluent, it is wavelength in 10mm of layer length. In a 220nm ultraviolet absorption spectrum The absorbance of 0.051 was shown and this hollow fiber film passed the above-mentioned criteria.
[0056] It is an effective film surface product in 9700 bundles about this hollow fiber film. The module for artificial kidneys of 2 was assembled 1.7m, and ethylene oxide gas sterilization, autoclave sterilization, and gamma ray sterility were respectively given to this module. Although there was almost no residual blood by hollow fiber lock out what performed ethylene oxide gas sterilization and autoclave sterilization when the module [finishing / these sterilization] was applied to the respectively same chronic-renal-failure patient and the residual blood condition (based on hollow fiber lock out) was compared, it was clearly much what gave gamma ray sterility. In addition, when the above-mentioned hollow fiber film was dissolved in chloroform, it saw, although gamma-ray-sterility processing was performed, and the insoluble solution component existed. It is thought that PVP structure-of-cross-linkage-ized this insoluble solution component, thereby, there is much residual blood and that to which anti-thrombus nature fell is presumed.
[0057] 17 % of the weight of 2PS examples, 20.4 % of the weight of PEG(s), and PVP1.7 Weight % and 60.9 % of the weight of DMA were mixed, heating stirring was carried out, and the uniform transparent undiluted solution was prepared. Outer diameter after it puts this undiluted solution for 16 hours and it carries out degassing at 45 degrees C 0.5mm, bore 0.25mm It extrudes in the air adjusted to discharge, 50 degrees C and 80% of relative humidity at 50 degrees C from the annular nozzle with the internal coagulation liquid which consists of 40 % of the weight of DMA, 0.3 % of the weight of PVP, and 59.7 % of the weight of water, and they are

after air transit of 10cm of dry zone length, and 12 m/min. It led to underwater [50-degree C], and made it solidify at a rate. Nozzle draft at this time It was 3.2. Subsequently, after being immersed for 5 minutes into 60-degree C warm water washing and 90 degrees C hot water processing, and a 90-degree C 6-% of the weight GURISENRIN water solution, it winds around a frame, and it dries, and is an outer diameter. 280 micrometers Bore 200 micrometers The hollow fiber film was obtained. In addition, this hollow fiber film has no conglutination yarn after desiccation, and it was able to manufacture to stability.
[0058] This film is 10000 shown in drawing 1 . In the outside-surface layer of a twice as many scanning electron microscope photograph (it is called a SEM photograph for short below) as this to the hollow fiber film, it is 0.05-1 micrometer. It was checked that much micropores exist. Moreover, 10000 shown in drawing 2 In the internal-surface compact layer of a twice as many SEM photograph as this to the hollow fiber film, it is width of face of 0.001-0.03 micrometers. It was checked that much slit-like micropores exist. 10000 which shows the cross section by the side of the SEM photograph in which the cross section of the 1500 times as many hollow fiber film shown in drawing 3 as this is shown, and the outside surface shown in drawing 4 A twice as many SEM photograph as this, 10000 which shows the cross section of the center section shown in drawing 5 10000 which shows the cross section by the side of the internal surface shown in twice as many a SEM photograph and drawing 6 as this From a twice as many SEM photograph as this Thickness to an internal-surface side 0.2-1 micrometer A compact layer is formed and an aperture is gradually expanded toward the center section of the film cross section. A membranous center section is 1-3 micrometers. Network structure side and outside-surface side 0.1-0.3 mum It was checked that it is the film of the unsymmetrical structure which consisted of layers which consist of precise network structure. Permeable ability of the obtained hollow fiber film PVP and PEG are each in 300 l/m2 and hr- (kg/cm2) and the film. The weight ratio of PVP and PS which those of exists and exists in an internal-surface compact layer 3.5% of the weight is the ratio of the weight ratio of PVP which exists in 23/77 and an internal-surface compact layer, and the weight ratio of PVP which exists in an outside-surface layer. It was 2.1. [2.2]
[0059] 17 % of the weight of 3PS examples, 34.0 % of the weight of PEG(s), 0.4 % of the weight of PVP, and DMA 48.6 Mixed heating stirring of the weight % was carried out, and the uniform transparent film production undiluted solution was prepared. Outer diameter after it puts this film production undiluted solution for 16 hours and it carries out degassing at 45 degrees C It extruded from 0.5mm and an annular nozzle with a bore of 0.25mm in the air adjusted to discharge, 50 degrees C, and 80% of relative humidity at 50 degrees C with the internal coagulation liquid which consists of 40 % of the weight of DMA, 1.5 % of the weight (the product made from GAF, K-120, and weight average molecular weight 250 10,000) of polyvinyl pyrrolidones, and 58.5 % of the weight of water. After air transit of 10cm of dry zone length, and 12 m/min It led to underwater [50-degree C], and made it solidify at a rate. Nozzle draft at this time It was 3.2. Subsequently, after being immersed for 5 minutes into 60-degree C warm water washing and 90 degrees C hot water processing, and a 90-degree C 5-% of the weight GURISENRIN water solution, it winds around a frame and dries, and it is an outer diameter. 280 micrometers Bore 200 micrometers The hollow fiber film was obtained. Permeable ability of the obtained hollow fiber film PVP and PEG are each in 400 l/m2 and hr- (kg/cm2) and the film. The ratio of the weight ratio of PVP to which the weight ratio of PVP and PS which that of exists and exists in an internal-surface compact layer 2.8% of the weight exists in 32/68 and an internal-surface compact layer, and the weight ratio of PVP which exists in an outside-surface layer was 16.5. [2.2] In addition, this hollow fiber film has no conglutination yarn after

desiccation, and it was able to manufacture to stability.
[0060] 17 % of the weight of 4PS examples, 20.4 % of the weight of PEG(s), 1.7 % of the weight (it is called "PVP/VA" for short the product made from GAF, S630, and the following) of vinyl pyrrolidone and vinyl acetate copolymers, and 60.9 % of the weight of DMA -- mixed heating stirring -- carrying out -- homogeneity -- the transparent undiluted solution was prepared. Outer diameter after putting for 16 hours and carrying out degassing at 45 degrees C It extruded from 0.5mm and an annular nozzle with a bore of 0.25mm in the air adjusted to discharge, 50 degrees C, and 80% of relative humidity at 50 degrees C with the internal coagulation liquid which consists of 40 % of the weight of DMA, 0.5 % of the weight of PVP/VA, and 59.5 % of the weight of water. After air transit of 10cm of dry zone length, and 12 m/min It led to underwater [50-degree C], and made it solidify at a rate. Nozzle draft at this time It was 3.2. Subsequently, after being immersed for 5 minutes into 60-degree C warm water washing and 90 degrees C hot water processing, and a 30-degree C 10-% of the weight ethanol water solution, it winds around a frame, and it dries, and is an outer diameter. 280 micrometers Bore The 200-micrometer hollow fiber film was obtained. Permeable ability of the obtained hollow fiber film 480 l/m2 and hr- (kg/cm2), PVP/VA and PEG are each in the film. 2.1 % of the weight exists 3.2% of the weight. The weight ratio of PVP/VA and PS which exists in an internal-surface compact layer is the ratio of the weight ratio of PVP/VA which exists in 21/79 and an internal-surface compact layer, and the weight ratio of PVP/VA which exists in an outside-surface layer. It was 1.7. In addition, this hollow fiber film has no conglutination yarn after desiccation, and it was able to manufacture to stability.
[0061] Mixed heating stirring of 17 % of the weight of 5PS examples, 10.2 % of the weight of PEG(s), 1.7 % of the weight of PVP, and the 71.1 % of the weight of the DMA was carried out, and the uniform transparent undiluted solution was prepared. Outer diameter after putting for 16 hours and carrying out degassing at 45 degrees C It extruded from 0.5mm and an annular nozzle with a bore of 0.25mm in the air adjusted to discharge, 50 degrees C, and 80% of relative humidity at 50 degrees C with the internal coagulation liquid which consists of 40 % of the weight of DMA, 0.5 % of the weight of PVP, and 59.5 % of the weight of water. It led to underwater [50-degree C], and made it solidify at the rate of 12 m/min after air transit of 10cm of dry zone length. Nozzle draft at this time It was 3.2. Subsequently, after being immersed for 10 minutes into 60-degree C warm water washing and 90 degrees C hot water processing, and a 80-degree C 8-% of the weight glycerol water solution, it winds around a frame, and it dries, and is an outer diameter. 280 micrometers Bore The 200-micrometer hollow fiber film was obtained. Permeable ability of the obtained hollow fiber film PVP and PEG are each in 260 l/m2 and hr- (kg/cm2) and the film. The weight ratio of PVP and PS which that of exists and exists in an internal-surface compact layer 2.8% of the weight is the ratio of the weight ratio of PVP which exists in 15/85 and an internal-surface compact layer, and the weight ratio of PVP which exists in an outside-surface layer. It was 1.9. [1.9] In addition, this hollow fiber film has no conglutination yarn after desiccation, and it was able to manufacture to stability.
[0062] Mixed heating stirring of 17 % of the weight of 1PS examples of a comparison, 34.0 % of the weight of PEG(s), and the 49.0 % of the weight of the DMA was carried out, and the uniform transparent undiluted solution was prepared. Outer diameter after putting for 16 hours and carrying out degassing at 45 degrees C It extruded from 0.5mm and an annular nozzle with a bore of 0.25mm in the air adjusted to discharge, 50 degrees C, and 80% of relative humidity at 50 degrees C with the internal coagulation liquid which consists of 40 % of the weight of DMA, and 60 % of the weight of water. After air transit of 10cm of dry zone length, and 12 m/min It

led to underwater [50-degree C], and made it solidify at a rate. Nozzle draft at this time It was 3.2. Subsequently, after performing 60 degrees C warm water washing and 90-degree C hot water processing and the mesenteriolum is immersed in the 90-degree C 10 % of the weight water solution of glycerols for 15 minutes, it winds around a frame, and it dries, and is an outer diameter. 280 micrometers, bore 200 micrometers The hollow fiber film was obtained. Permeable ability of the obtained hollow fiber film It was 800 l/m2 and hr- (kg/cm2).
[0063] 17 % of the weight of 2PS examples of a comparison, water 1.0 % of the weight and PVP 6.0% of the weight, mixed heating stirring of the 76.0 % of the weight of the DMA was carried out, and the uniform transparent undiluted solution was prepared. Outer diameter after putting for 16 hours and carrying out degassing at 45 degrees C It extruded from 0.5mm and an annular nozzle with a bore of 0.25mm in the air adjusted to discharge, 50 degrees C, and 80% of relative humidity at 50 degrees C with the internal coagulation liquid which consists of 40 % of the weight of DMA, and 60 % of the weight of water. After air transit of 10cm of dry zone length, and 12 m/min It led to underwater [50-degree C], and made it solidify at a rate. Nozzle draft at this time It was 3.2. Subsequently, after being immersed for 10 minutes into 60-degree C warm water washing and 90 degrees C hot water processing, and a 80-degree C 8-% of the weight glycerol water solution, it winds around a frame, and it dries, and is an outer diameter. 280 micrometers Bore The 200-micrometer hollow fiber film was obtained. Permeable ability of the obtained hollow fiber film The weight ratio of PVP and PS which 5 % of the weight of PVP exists in 80 l/m2 and hr- (kg/cm2) and the film, and exists in an internal-surface compact layer is the ratio of the weight ratio of PVP which exists in 16/84 and an internal-surface compact layer, and the weight ratio of PVP which exists in an outside-surface layer. It was 0.7. In addition, this hollow fiber film had very much conglutination yarn after desiccation, and it was not able to manufacture it to stability.
[0064] It extruded using the undiluted solution of example of comparison 3 example 2 in the air adjusted to discharge, 50 degrees C, and 80% of relative humidity at 50 degrees C with the internal coagulation liquid which consists of 40 % of the weight of DMA, and 60 % of the weight of water. After air transit of 10cm of dry zone length, and 12 m/min It led to underwater [50-degree C], and made it solidify at a rate. Nozzle draft at this time It was 3.2. Subsequently, after being immersed for 5 minutes into 60-degree C warm water washing and 90 degrees C hot water processing, and a 90-degree C 6-% of the weight glycerol water solution, it winds around a frame, and it dries, and is an outer diameter. 280 micrometers Bore The 200-micrometer hollow fiber film was obtained. For the permeable ability of the obtained hollow fiber film, PVP and PEG are each in 600 l/m2 and hr- (kg/cm2) and the film. Weight ratio of PVP and PS which that of exists and exists in an internal-surface compact layer 3.0% of the weight Ratio of the weight ratio of PVP which exists in 8/92 and an internal-surface compact layer, and the weight ratio of PVP which exists in an outside-surface layer It was 0.8. [2.1]
[0065] It winds around a frame, the hollow fiber film obtained by the approach of example of comparison 4 example 2 is dried, without being immersed into a glycerol water solution, after [60 degrees C] carrying out warm water washing and performing 90-degree C hot water processing, and it is an outer diameter. 280 micrometers Bore 200 micrometers Although the hollow fiber film was obtained, there was much conglutination of the hollow fiber film after desiccation, and it was not able to manufacture to stability. Moreover, permeable ability of the obtained hollow fiber film There is a problem practically very as low as 125 l/m2 and hr- (kg/cm2).
[0066] Mixed heating stirring of 17 % of the weight of 6PS examples, 22.0 % of the weight of

PEG(s), 1.7 % of the weight of PVP, and the 59.3 % of the weight of the dimethylformamides was carried out, and the uniform transparent undiluted solution was prepared. Outer diameter after putting for 16 hours and carrying out degassing at 45 degrees C 0.7mm, bore From the 0.3mm annular nozzle, it extruded at 30 degrees C in discharge, 80% of relative humidity, and the air adjusted to 50 degrees C with the internal coagulation liquid which consists of 59.5 % of the weight of dimethylformamides, 0.5 % of the weight of PVP, and 40 % of the weight of water. After air transit of 10cm of dry zone length, and 10.5 m/min It led to underwater [50-degree C], and made it solidify at a rate. Nozzle draft at this time It was 3.8. Subsequently, 60 degrees C warm water washing and 90-degree C hot water processing, and 75 degrees C After being immersed for 10 minutes into a 7.5-% of the weight glycerol water solution, it winds around a frame, and it dries, and is an outer diameter. 360 micrometers Bore 230 micrometers The hollow fiber film was obtained. For the permeable ability of the obtained hollow fiber film, PVP and PEG are each in 850 l/m2 and hr- (kg/cm2) and the film. The weight ratio of PVP and PS which that of exists and exists in an internal-surface compact layer 2.7% of the weight is the ratio of the weight ratio of PVP which exists in 20/80 and an internal-surface compact layer, and the weight ratio of PVP which exists in an outside-surface layer. It was 3.0. [1.8] In addition, this hollow fiber film has no conglutination yarn after desiccation, and it was able to manufacture to stability.

[0067] It is an effective film surface product in 9700 bundles about the hollow fiber film obtained in example 7 examples 2, 3, and 5 and the examples 1-3 of a comparison. The module for artificial kidneys of 2 was assembled 1.7m. These all performed autoclave sterilization in the wet condition. UFR (ultrafiltration rate) and the dialysis engine performance were measured based on the performance-evaluation criteria of Japanese Society for Artificial Organs using this module. Moreover, measurement of the screen multiplier of albumin and an inulin is the approach (kidney and dialysis separate volume 27 167 (1989)) shown in high performance membrane study group. It carried out. A measurement result is shown in Table 1. From Table 1, examples 2, 3, and 5 were excellent in all, such as dialysis engine performance, and, moreover, residual blood (based on lock out of a hollow fiber) was excellent in anti-thrombus nature few. On the other hand, although the example 1 of a comparison is excellent in all, such as dialysis engine performance, a problem is in anti-thrombus nature. Moreover, the examples 2 and 3 of a comparison had the low dialysis engine performance, and there was a problem also in anti-thrombus nature.

[0068]

[Table 1]

	C urea. (ml/min)	C inu. (ml/min)	S c Alb.	S c inu.	UFR 注1	残血状態 注2
実施例 2	190	103	0.001	0.99	6.4	◎
実施例 3	191	110	0.001	0.99	9.1	◎
実施例 5	185	98	0.001	0.97	5.1	○
比較例 1	195	128	0.002	0.99	17.5	×
比較例 2	158	57	0.000	0.48	2.3	△
比較例 3	192	89	0.000	0.95	12.1	×

[0069]
urea; A urea, an inu. inulin, and Alb; albumin notes 1 unit: -- ml / (min, m2, and mmHg) notes 2 residual blood: -- O; -- almost -- nothing and O; ** **; -- many [a little] x; -- **

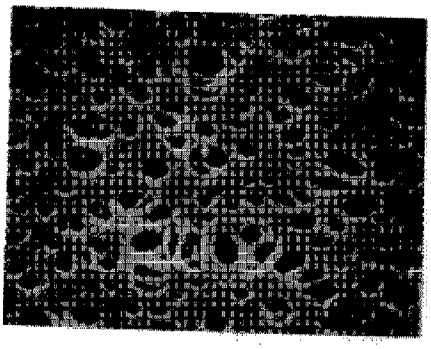
DESCRIPTION OF DRAWINGS

[Brief Description of the Drawings]
[Drawing 1] It is the 10000 times as many SEM photograph in which the structure of the outside-surface layer of the polysulfone system hollow fiber film obtained in the example 2 is shown as this.
[Drawing 2] 10000 which shows the structure of the internal-surface compact layer of the above-mentioned hollow fiber film It is a twice as many SEM photograph as this.
[Drawing 3] It is the 1500 times as many SEM photograph in which the cross-section structure of the above-mentioned hollow fiber film is shown as this.
[Drawing 4] 10000 which shows the cross-section structure by the side of the outside surface of the above-mentioned hollow fiber film It is a twice as many SEM photograph as this.
[Drawing 5] 10000 which shows the cross-section structure of the center section of the above-mentioned hollow fiber film It is a twice as many SEM photograph as this.
[Drawing 6] 10000 which shows the cross-section structure by the side of the internal surface of the above-mentioned hollow fiber film It is a twice as many SEM photograph as this.

DRAWINGS

[Drawing 1]

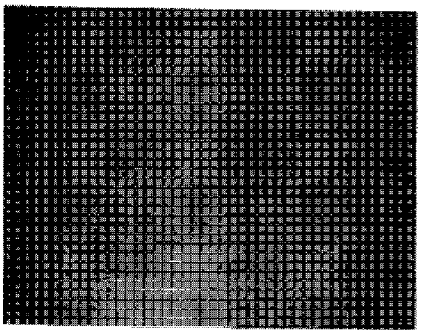
図面代用写真



(写真)

[Drawing 2]

図面代用写真



（写真）

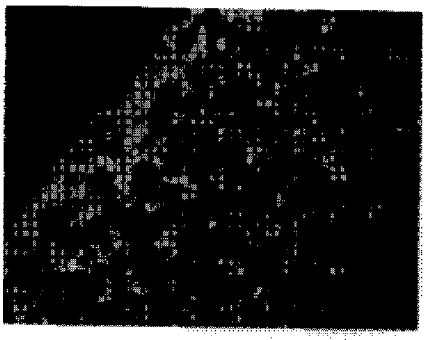
[Drawing 3]

図面代用写真

（写真）

[Drawing 4]

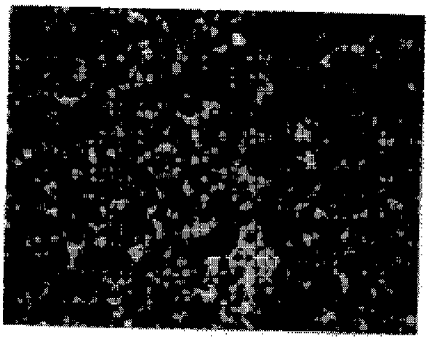
図面代用写真



（写真）

[Drawing 5]

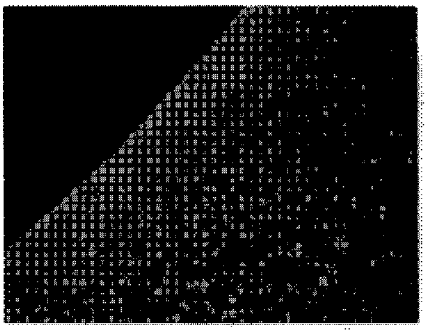
図面代用写真



(写真)

[Drawing 6]

図面代用写真



(写真)

CORRECTION OR AMENDMENT

[Kind of official gazette] Printing of amendment by the convention of 2 of Article 17 of Patent Law
[Section partition] The 1st partition of the 2nd section
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69/08

[Procedure revision]
[Filing Date] June 5, Heisei 10
[Procedure amendment 1]
[Document to be Amended] Specification
[Item(s) to be Amended] Claim 9
[Method of Amendment] Modification
[Proposed Amendment]
[Claim 9] The solution which has a poor solvent operation to the above-mentioned polysulfone system polymer is water, alcohols, ethylene glycol, propylene glycol, a glycerol, and weight average molecular weight. The manufacture approach of the polysulfone system hollow fiber film given in claim 6 thru/or any of 8 they are. [which is at least one sort of liquids chosen from the group which consists of 600 or less polyethylene glycol]

[Translation done.]